American Journal of Diseases of Children

VOLUME 64 OCTOBER 1942 NUMBER 4

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ANXIETIES OF CHILDREN

THEIR CAUSES AND IMPLICATIONS

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In a discussion of the anxieties of childhood one can visualize a reunion at the cross roads of the pediatrician, the psychiatrist and the progressive educator. And as they exchange views it becomes apparent that they have all learned a great deal about children since they went their independent ways some fifteen or twenty years ago. They are now in complete agreement on the following basic principles: First, the anxieties of adulthood are largely, if not entirely, but a renewal of anxieties which took definite form during adolescence, and the anxieties of adolescence are but a repetition and expansion of the anxieties of the first three years of life. Second, the greatest hope for better health lies in prophylaxis. Third, it follows, then, that the problem of mental health is primarily for pediatric concern and one does not have to apologize before this society for a discussion of mental ill health, its causes and treatment.

The extreme anxiety states, usually designated as neuroses, were described as observed in adults by Freud over forty years ago. More recently these same conditions have been recognized in children and have been reported by Langford,[1] Barrett,[2] Pearson [3] and many others. Originally thought to be rare or nonexistent in children, they are now known to be fairly common, as evidenced by the fact that I have observed 10 children with extreme forms in the past two and one-half years. Most pediatricians do not actively treat these patients, preferring to send them to child psychiatrists. All pediatricians are interested in the preventive therapy, however, because they are the only physicians who see children before and at the onset of symptoms. This paper concerns itself, therefore, with a description of anxieties and of the specific and general fac-

Read before the American Pediatric Society, Skytop, Pa., May 2, 1942.

1. Langford, W.: Anxiety Attacks in Children, Am. J. Orthopsychiat. **2**:210-218 (April) 1937.

2. Barrett, W. G.: A Childhood Anxiety, Psychoanalyt. Quart. **6**:530-535 (Oct.) 1937.

3. Pearson, G. H. F.: A Case of Compulsion Neurosis in an Eleven Year Old Boy, Am. J. Orthopsychiat. **10**:136-151 (Jan.) 1940.

tors which, with their implications, may be the causes of mental ill health. I am describing the extreme conditions because they are the most spectacular and bring out the etiologic factors more vividly, but I recognize that the milder forms of the syndrome are far more common. The following cases are illustrative.

REPORT OF CASES

CASE 1.—Mary E., an 11 year old girl, was referred by Dr. A. H. Parmelee because of "emotional disturbances, loss of weight and anorexia." Eighteen months previously she had had an infection of the respiratory tract with otitis media, but she promptly recovered. A couple of weeks later she received the first prophylactic inoculation against scarlet fever. With succeeding inoculations the reactions became more severe, and she was frightened by the procedure, vomiting immediately after the third inoculation. At about this time a girl who was a friend of the patient died of peritonitis following rupture of the appendix. The patient was unusually disturbed by this event. She had anorexia, began to lose weight, bit her nails, cried easily, indulged in temper tantrums for the first time in her life, did poorly in school and began to complain of abdominal distress. A physician was called, and he suspected incipient chorea. She improved somewhat and went to summer school (six months after the first symptoms). The following fall she seemed weak and tired. Her school work was poorer, and she was bothered by noises. She began having more severe attacks of abdominal pain and expressed fears of illness and particularly of appendicitis. These spells soon reached hysterical proportions. She cried bitterly, became pale and trembled, and her parents had difficulty in controlling her. At this time she was seen by Dr. Parmelee. He placed her in a hospital for observation but could find no evidence of abdominal disease and concluded that an emotional disturbance was the cause of the trouble.

One attack was observed in the office. Mary was talking about her mother, who was away from home on a short trip. She stopped talking and then said, "I want to go home; I am getting sick." She became pale and wept; her whole body trembled. She complained of abdominal distress and expressed a fear of illness.

On succeeding visits to the office she became cooperative. As her confidence was obtained and she expressed herself freely, she got the most satisfaction from her expressions of resentment toward her family. She created a family, drew pictures of the members and pointed out the "mean" father, mother and younger brother. She liked to shoot darts from a gun at members of her imaginary family and killed each of them hundreds of times. During her first visits this was an imaginary family; later she admitted she was expressing her feelings toward her own family and finally spoke of them as "my mean mother, my old father and my darn brother." During this time (about five months) her attacks slowly subsided, her appetite returned and she was able to do good school work again. She began to fight more with her brother and talked back to her parents the way a normal child should. She finally described her attacks as beginning when she hated her mother, father and brother. She had been taught that these feelings were bad. When they came into her mind, she experienced a "funny feeling in her abdomen and became scared that she would get sick and die."

Further light on the origin of the emotional disturbance was shed by a more detailed family history obtained in subsequent interviews with her mother. Mary was the first child. Her father told no one about her birth, and it was not known to his friends until it was announced in the town newspaper three days later. The father wanted a boy, refused to show any interest in his daughter and never

gave her the consideration or attention a child requires. Her mother was "nervous." She was a physician's daughter—used to every material thing she wanted—but her own father had been very strict, and her mother "was sick all of the time" (probably neurotic). She did not marry until late, and relations with her husband were never satisfactory. She gave her baby (the patient) a great deal of attention but was resentful about her own lot in life. She followed a very strict schedule with the child and was exacting in her training program. Her success in completely "breaking" the patient is evidenced by the fact that Mary was a good child who did not indulge in displays of temper until after the onset of her acute psychologic illness.

The brother was born when the patient was 2 years of age. He was accepted wholeheartedly by his father and each year occupied a more important place in the family. The training program for him was less severe, and in his growth and development the parents had common interests. All of these factors added to the fears and resentments of the patient.

Summarizing the obvious important factors (I have left out many important details) which contributed to this girl's psychologic illness, one finds: (1) lack of a sense of security in her parents because she was rejected by her father and accepted with mixed emotions by her mother; (2) a strict program under the guise of attention to health during infancy; (3) the attempt to inflict adult standards of behavior on her during late infancy to the extent that she was completely broken; (4) jealousy of her brother (these conditions stimulated fears and resentments in the patient's mind); (5) the death of a playmate, and (6) the combined sense of guilt due to hating the members of her family, a feeling which she had been taught was bad, and fear of punishment for being bad, which was emphasized by the death of her playmate.

In the behavior of this girl one sees all of the signs and symptoms of the panic as found in the neurosis of an adult. Panics are always divided into two parts: In the first, fears, usually subconscious or at least not recognized by the patient, develop and cause symptoms referable to the sympathetic nervous system; in the second, the patient becomes afraid of those symptoms and apprehensive that he will get sick and die. These fears and confusions make up the panic. The primary anxiety is due to a sense of guilt—the fear of hate. This was described vividly by this patient.

The treatment consisted of gaining the patient's confidence so that she could express her hates and rationalize them. This is largely a matter of reeducation. She learned that her resentments were understandable and did not result in punishment. The treatment was the more effective because the parents were able to understand the nature of the illness and to understand their own problems well enough to give the patient the security she had missed. They recognized further that their standards of conduct for her were too high and adjusted them to her level of growth. Mary no longer has panics. She is doing well in school, and to all outward appearances she is entirely well. Actually she will never entirely recover. The harm from the insecurity during infancy can never be cured. The emotional suppression caused by rigid schedules and discipline has left permanent scars on her personality. She will always be easily frightened. A part of the treatment consisted in teaching her that people get scared easily and that when they are scared they sometimes have abdominal distress and many other symptoms similar to those of organic illness.

It is unnecessary to describe the other cases in detail. They are monotonously alike. Perhaps a brief summary of the important factors will be interesting.

CASE 2.—H. S., a 12 year old girl, was referred by Dr. Robert Black because of "spells" during which she became nauseated and fearful that she would get sick and at times even that she would die. These periods of anxiety had begun about five years previously and had been intermittent since that time. The first one occurred soon after the death of the mother of one of the boys in her room in school.

The patient was able to analyze her attacks of nausea and intense fear. She noted that "a peculiar kind of fear makes me nauseated and then I get scared

Summary of Cases Reported

Case: Sex; Age at Onset	Precipitating Condition	Parental Attitude	Schedule in Infancy	Result of Training Program	Primary Fear	Outstanding Symptom	Panic
1, F 9½	Death of friend	Rejection (father), apprehension (mother)	Rigid	Broken	Hate of father, mother and brother	Abdominal distress	Fear of illness and death
2, F 7	Death of mother of schoolmate	Extreme apprehension	Rigid	Broken	Hate of mother	Nausea	Fear of illness and death
3, F 9	Sex instruction	Rejection (mother)	Rigid	Broken	Hate of mother, fear of sex	Nausea and vomiting	Fear of illness
4, M 10	Death of friend	Rejection, apprehension	Rigid	Broken	Hate of mother, father and friend	Trembling	Fear of being killed
5, M 9	.....	Extreme apprehension	Semi-rigid	Broken	Hate of father, mother and brother	Pain in the joints and extremities	Illness and death
6, F 8	Death of sister	Rejection	?	Broken	Hate of mother and sister	Abdominal pain	Fear of T. B.; meningitis
7, F 9½	.....	Rejection, apprehension	Rigid	Broken	Hate of mother and brother	Trembling and crying	Impending danger
8, F 10	.....	Rejection	Rigid	Broken	Hate of mother and sister	Trembling and abdominal pain	Illness
9, F 8	Exhibitionism? fear of teacher	Rejection	Rigid	Broken	Hate of family and teacher	Inability to recite in school	Suffocation
10, F ½	?	Apprehension, rejection	Rigid	?	?	?	?

something awful will happen to me." Later she described intense resentment toward her mother and stated that she would often bite herself at times when the feeling was pronounced. She had many dreams in which her mother was being killed or was dying from some other cause. Finally she recognized that the "peculiar fear" and abdominal distress came into her mind when she hated her mother.

The mother was an unstable, neurotic woman who was apprehensive over the welfare of her only child. The patient was a well behaved quiet little girl, but she never ate enough to please her mother. The mother often told her that she (the mother) would get sick because the child would not eat more food. After the death of the mother of a classmate, the patient became afraid that her own mother would die. Her sense of guilt from feeling hate toward her own mother increased, and she was increasingly terrified that she would be punished for feeling the way she did.

The anxieties disappeared when the patient was able to rationalize her resentments. Her whole personality changed at the same time from that of a quiet, asocial girl to a moderately aggressive, friendly person.

CASE 3.—P. W., a 10 year old girl, was referred by Dr. C. A. Aldrich because of abdominal pain of two years' duration, hysterical outbreaks at the mention of leaving home and continual vomiting during a time when she was away from home for six months. Even though expert pediatric advice was available to the parents, feeding the patient had been a problem nearly all of her life. There was the further history that she screamed and fought when she was put on the toilet in infancy and that she had been afraid of airplanes, of the dark and of many other things. When she was 3 years of age, her mother said "she would make a little lady out of her or kill her." The mother was socially ambitious and insisted on having a polite little girl who would act properly before guests.

In the office the child was cooperative only while playing games involving the killing of people. Later she expressed extreme resentment toward her mother and grandmother, but she felt that she was a bad girl for hating them. She recognized that this sense of guilt because of hating them gave her a "funny" feeling in the abdomen. The vomiting developed after she had attended classes in sex education at school, from which she became afraid of the process of having babies. This information increased her sense of guilt due to her hatred of her mother, because she felt her birth could have caused the mother's death. In addition, sex was something bad and nauseating to her.

CASE 4.—M. Y., a 10 year old boy, was referred by Dr. Herman Meyer because of "spells" in which he became terrified; he felt that there was some one after him. The first attack came on a few hours after he regained consciousness from an operation on one of his eyes. He had been especially tense, however, for several weeks before the operation—since a boy who was a close friend had drowned.

In the anxiety attacks the patient imagined that spirits were after him and were going to kill him. The mother of the friend who had died had explained to him that her son was dead but that his spirit was still among them. This disturbed the patient because he had fought the boy frequently; he felt very guilty about it after his friend died and feared that his spirit might get him and punish him.

There were many more important factors in the family history. The patient's mother was an apprehensive woman, who had been under medical care for years because of neurotic complaints. His father was an alcoholic addict, and there were constant differences between his parents. Because of these differences his mother had not wanted a baby; his conception "was an accident." He was reared under a strict schedule and was a good, obedient boy. In addition to the sense of guilt due to his resentments toward the friend that died, he was resentful of both parents and thought he was a bad boy for having these thoughts. In his panics he feared that ghosts were going to kill him in order to punish him for this badness.

CASE 5.—M. B., a 12 year old boy, was referred to the behavior clinic of the Presbyterian Hospital from the Cook County Hospital by Dr. Maurice Blatt. For the preceding three years he had complained frequently of pains in various parts of his body. He thought he had rheumatism and would get heart disease and die. This information was given the parents by a physician who saw him when he first complained of the pains. Laboratory and clinical studies revealed no evidence of organic disease.

Melvin was the older of two children. His mother had a nervous breakdown soon after he was born. She was an apprehensive woman and was always concerned over her own health and that of the boy. Both parents were very strict.

After several miscarriages his mother gave birth to a second child when the patient was 8 years of age. The new baby became the center of the home. The patient was forced to go to bed early in order to get enough rest, because his brother awoke at 6 a. m.; he had to play with his little brother and was rebuked for any show of resentment.

The patient at first spent much time telling how he loved his mother, father and brother, but as his confidence was gained he complained of the ill treatment he received at home. He finally related that he got pains after his mother beat him and took his allowance away because he would not play with his brother. He also described peculiar thoughts—in which he imagined his mother, father and brother would get sick. He later recognized these thoughts as day dreams and expressions of resentment. These feelings and ideas were always accompanied by pains and the fear of severe illness. He finally recognized that the pains were "funny feelings" in various parts of his body when he felt resentful. It took many weeks to convince him that a feeling of hate was normal and would not bring punishment on him. His improvement paralleled his acceptance of the idea that his feelings were normal.

CASE 6.—S. R., a 10 year old girl, was referred to the behavior clinic of the Presbyterian Hospital from the Children's Memorial Hospital. For two years she had "attacks" during which she cried bitterly, complained of stomachache and expressed the fear that she would get tuberculous meningitis. A younger sister had died of that disease two and a half years previously.

The patient was the second of 4 children. The mother stated frankly that she had never felt the same toward this child as toward the two younger children. This mother also believed children "should mind." The girl was obedient until she was 6 or 7 years of age, but after that she would not help her mother with the work or do as she was told. She had especially resented having to take care of the sister that died.

Her mother noted that the patient was "more nervous" after the death of her sister. The first attack (pains) came on while her mother was away from home. The patient was slowly able to analyze the pains without suggestions from the examiner. She would think of her sister, feel bad because she used to hate her and think she would be punished for having such bad thoughts. Then she would have abdominal distress and fear she would get tuberculous meningitis and die. These attacks usually came on after she had been criticized by her mother.

CASE 7.—M. W., a 10 year old girl, came for examination because of "spells" of crying during which she trembled all over, said she was scared and knew something was going to happen to her. Her first attack came on six months previously while she was saying her prayers at night. The spells usually occurred at night but sometimes came on at other times of the day. Occurring about once a week at first, they had increased in frequency until she was having two or three a day.

The patient was the first child. The parents were incompatible from the time of their marriage, and the father was opposed to having children. Her mother was excitable and apprehensive. The patient looked and acted like her father, which was a source of resentment to the mother. The mother stated that she could never feel toward the patient as she did toward the patient's brother, four years younger, who looked like his mother. Ellen was reared under a very strict schedule. She became a good little girl; she was quiet, obedient and mannerly. The only problem her mother had was her resentment toward her brother.

As previously stated, the first spell came on while the patient was saying her prayers. She gave the reason, namely, the ideas "I hate my mother, I hate my

brother, I hate everybody." These compulsive thoughts gave her a feeling of weakness and dizziness, and she became afraid that something was going to happen to her. The treatment consisted in reeducating her to the point where she could accept her resentments as normal.

CASE 8.—L. R., a 10 year old girl, came in with abdominal pain and crying spells. Her history was about identical with that of the patient of case 7. Her pains were initiated by compulsive thoughts "I hate you."

CASE 9.—M. B., a 17 year old girl, was referred by Dr. L. P. River because of poor school work, outbreaks of temper at home and asocial behavior. The personal history revealed that when called on in school she had attacks in which there were a feeling of constriction in her chest and throat, "trembling inside" and fear of losing her voice and of being suffocated. These "spells" began when she was about 8 years of age, but she had never told any one about them. They began about the time she saw a boy expose himself. Mary was the only child. Her mother married very late; she was 44 years old and the father was over 50 years of age when the patient was born. The child was reared by an extremely domineering, resentful, neurotic grandmother while both parents worked. A rigid schedule was forced on her. She was not allowed to play with other children until she entered school and was not allowed to feed herself until she was 8 years of age. She was described as an attractive, obedient little girl until she was 9 years of age. Her mother "never cared for marriage or children."

The patient was uncooperative in the office for many weeks. As soon as she discovered that her visits were confidential and that she could express herself freely, many visits were spent expressing resentments toward her grandmother and finally toward her parents for giving her little attention. As in all the previous cases her fear of hating her family created the greatest confusion in her mind. In going back to the beginning of her anxiety attacks she recalled that they began when she had a teacher whom she did not like, and, being in a parochial school, she was as much concerned over these resentments as those toward her family. Her rapid improvement began with the expression of these resentments and the assurance that one could not help feeling the way she did. A good girl, she reported to her mother only "The doctor taught me things worth a million dollars. I am going to pay him myself when I finish high school and get a job."

CASE 10.—Sarah B. is 4 months of age. Her mother's attitude attracted the attention of the obstetrician during pregnancy; he found that she complained a great deal about trivial matters and after the baby was born exaggerated the seriousness of problems that concerned the baby. Sarah's mother believes that children should not be spoiled. The mother's attitude becomes especially important when, in confidence, she states that "she does not like babies and does not feel right about Sarah." Unless her attitude can be corrected, one can predict that this baby will grow up to be a neurotic woman. Does this not place a great responsibility on the pediatrician?

COMMENT

In reviewing these cases as a group, many important facts become obvious. They are all monotonously alike. Here is a group of children, mostly girls, all of normal intelligence and nearly all of them having panics such as one encounters in the neurotic adult. As in the adult, the panics are made up of primary fears, of which the patient may not be aware but which give rise to any combination of symptoms referable

to the sympathetic nervous system, and secondary fears, which are apprehension of the symptoms themselves. This combination of fears gives rise to feelings of confusion which complete the panic.

In all of the patients fear of hate was the most disturbing feeling and usually stimulated the primary fear. These were all good children, meaning that they were "broken" and were taught that it is bad to hate any one. Then when strong resentments developed, which were usually toward those they loved the most, they developed a strong sense of guilt, which gave rise to the primary anxiety, and this emotional disturbance stimulated the sympathetic nervous system.

There was unquestioned rejection of the child by one or both parents in most of the cases and extreme fear of the parents in the other cases. In no case did the parents' attitude approach normal. In other words, the patients were insecure; none of them had the first essential for mental health, namely, security in his parents.

Nearly all of the patients were on a strict schedule during infancy, and all of them were held to impossible standards of conduct during their early childhood. In being "broken," they had their normal initiative, originality, aggressiveness and emotions suppressed, and their fears and resentments were not expressed outwardly but were turned in on themselves.

There was usually an experience of an alarming nature which precipitated the mental illness, but these frights were not the primary or main cause of the condition. Too often one blames a single experience for causing a mental illness. Whether or not a child is disturbed by a given experience depends on the condition of his mind at the time. If he feels insecure and is lacking in self confidence he may react violently to a situation which would not have disturbed him had he felt secure in his parents and confident of himself.

There may be one additional factor in these conditions—namely, the type of response to unpleasant situations, which may be inherent in the baby. As has been pointed out by Dr. Charles A. Aldrich and Dr. Margaret Fries and others, the type of response to unpleasant situations varies in individual babies, and these individual patterns probably continue unchanged throughout life. It will require further observations to determine whether babies who later present the pattern of behavior called neurotic responded in a passive manner to difficulties in their environment from birth, in contradistinction to the aggressive, destructive reactions of other children under difficult circumstances.

The patients whose cases have been cited had severe mental illness, which is comparatively rare. Much more common is the sort of behavior presented by children (encountered by the pediatrician almost daily)

who have the family background and mild symptoms of the same condition. They are the children who will grow up into the much larger group of neurotic adults.

What is more important than the cases themselves is the generally accepted fact that a diagnosis of anxiety state or neurosis does not carry the implication of a specific disease; it is not a disease entity like scarlet fever, for example. In these patients with anxieties, one sees in exaggerated form conditions which are common in children. In these extreme anxiety states there is illustrated one kind of reaction to environmental conditions that are too difficult for the child. In them one may find the cause of mental ill health and recognize the essentials for mental health.

SUMMARY

Nine cases of extreme anxiety (neurosis) in children are recorded.

Like neurotic adults, these patients had panics with a primary fear (largely fear of hate) and a secondary fear of the symptoms produced by the stimulation of the sympathetic nervous system.

All of the children were rejected by their parents or had extremely apprehensive parents.

Nearly all of the children were subjected to a rigid schedule during infancy, and all of them were held to impossible standards during childhood. They were all "broken" children.

There was usually an alarming experience which precipitated the onset of the acute illness, but it was never the primary or main cause.

While reactions of this kind are comparatively rare, the factors causing them and milder forms of the condition are encountered daily.

Neurosis is not a disease entity; it is but an extreme reaction of one type.

From a study of these cases one may see the causes of mental ill health and learn the essentials of mental health.

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CONCOMITANCE OF CHRONIC ACIDOSIS WITH LATE RICKETS

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In all forms of chronic acidosis, regardless of cause, elimination of fixed base is increased. In some instances, increase in the elimination of fixed base is the primary cause of acidosis. Prolonged excessive loss of fixed base will deplete calcium reserves. According to the authors' concept, the development of rickets concomitant with chronic acidosis is due to the associated deficiency of base, regardless of other factors involved.

Chronic renal insufficiency is the commonest antecedent of rickets associated with chronic acidosis. The term "renal rickets" properly refers to the syndrome of impaired growth, static deformities of bone and rickets-like epiphysial changes seen in children with chronic renal insufficiency. In these children the underlying disturbance is dependent on structural changes within the kidney. Rickets, when present, is to be regarded as a sequel; its importance is overshadowed by the more serious limitation of renal function. Because of the irreversibility of the structural renal damage, treatment is palliative only, and the ultimate prognosis for life is poor. Yet even in these children amelioration of the acidosis by means of alkali therapy may result in decrease in the rickets and resumption of growth.[1]

Renal dysfunction may occur in the absence of anatomic disease of the kidney. The pattern of tubular function is altered, owing to extrarenal causes, in divergent conditions such as dehydration, intestinal obstruction, Addison's disease or diabetes insipidus. The altered function sometimes may be considered as compensatory, but it may give rise to harmful effects. Some of these effects may resemble superficially those of renal insufficiency with rachitic changes in the bones. In some instances the altered electrolyte balance may be compensated

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Presented before the American Pediatric Society, Hot Springs, Va., May 24, 1941.

1. Graham, G., and Oakley, W. G., The Treatment of Renal Rickets, Arch. Dis. Childhood **13**:1 (March) 1938.

through therapy; when rickets arises owing to deficiency of base, therapy with maintenance amounts of base may be expected to heal the rickets, prevent further deformity and add greatly to the patient's comfort, even though the underlying disorder may not be altered through such treatment.

Studies of 3 children with late rickets and imbalance of acid-base metabolism have been reported previously from this clinic.[2] In 1 of these, rickets was healed through the regular ingestion of sodium bicarbonate. A fourth patient, with late rickets and chronic acidosis, was observed intermittently in this department for three years, during which time her rickets and osteoporosis healed and remained so under base therapy. Concurrently, most of her metabolic anomalies were controlled and the electrolyte values restored toward normal levels. Following is a summary of her record.[3]

REPORT OF A CASE

This girl of 11½ years came to the hospital in January 1933 because of weakness and difficulty in walking of four years' duration and of progressive severity. She had become clumsy in her movements, had found it impossible to be normally active and finally was unable to climb stairs. During the six months prior to the initial examination she had acquired right valgus and left varus deformities of the knees. During the course of her disability she had experienced occasional brief attacks of tingling and numbness in her extremities. The earlier medical history was uneventful. Growth had not been notably impaired, and at the time of examination she weighed 86½ pounds (99.3 Kg.) and was 54½ inches (137.3 cm.) tall, essentially of average height and weight for her age.

The physical examination did not offer evidences of noteworthy organic disease other than that of the osseous system. Static deformity of the legs was present, as has been described (fig. 1 *A*). Bulbous enlargement was noted at the cartilaginous zone of many bones, especially the wrists and ankles. Roentgenograms revealed active rickets with subnormal mineralization of the shafts of long bones (fig. 2 *A*). The calcium content of the serum was 10.6 mg., and the inorganic phosphorus 3.1 mg. per hundred cubic centimeters; the phosphatase amounted to 71.5 Jenner-Kay units per hundred cubic centimeters. Tuberculin and Wassermann tests gave negative results. The basal metabolic rate was within the lower limit of normal. The blood pressure was not increased. Urologists were unable to find evidences of renal lesion or dysfunction.

The child was admitted to the hospital for study. It was observed that the daily volume of urine was about twice normal, although she experienced no

2. (*a*) Boyd, J. D.: Chronic Acidosis Secondary to Ureteral Transplantation, Am. J. Dis. Child. **42**:366 (Aug. 1931.) (*b*) Boyd, J. D., and Stearns, G.: Late Rickets Resembling the Fanconi Syndrome, ibid. **61**:1012 (May) 1941.

3. Certain of the biochemical data relating to this patient were reported previously (Stearns, G., and Warweg, E.: Studies of Phosphorus of Blood: Phosphorus Partition in Blood of Children with Disease, Am. J. Dis. Child. **50**: 1164 [Nov.] 1935).

frequency of urination; in fact, she voided infrequently, but each voiding was of large volume. The specific gravity of the urine was low and varied only 4 points during the twenty-four hours. Moreover, the reaction of the urine was neutral when voided, and subsequent studies indicated inability of the child to secrete acid urine. The daily excretion of ammonia was normal in amount and in proportion to the total excretion of nitrogen. The urea clearance was unimpaired, and 62 per cent of phenosulfonphthalein was eliminated in two hours. Albuminuria was noted initially but could not be demonstrated once therapy was established. The nonprotein nitrogen content of the blood was 47 mg. per hundred cubic centimeters. Aside from the levels of phosphorus and of phosphatase, the most striking characteristics of the blood were the marked lowering of chloride content and of alkali reserve, each of which was only about half of the usual amount (table 1).

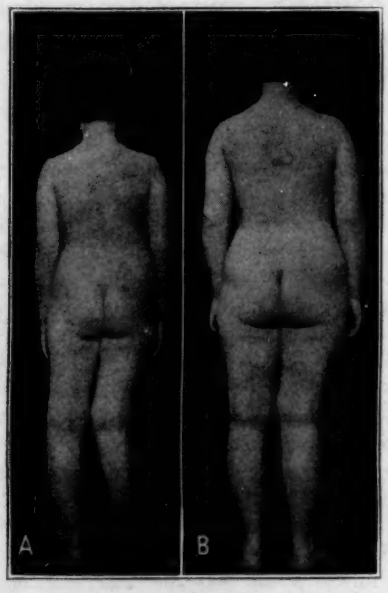

Fig. 1.—Photograph of child with chronic acidosis and secondary active rickets: (*A*) at time of first observation; (*B*) three years later, after continued medication with sodium bicarbonate. Note degree of spontaneous correction of deformities of legs and normality of growth and maturation.

Most of the abnormalities noted would have remained undiscovered with the usual procedures of clinical examination and of rationalization. Rachitic deformities seen in children usually are considered to be residual to active rickets in infancy, rather than indicative of current activity. With active rickets demonstrated through the roentgenogram and low serum phosphorus established through biochemical analysis, the patient's condition might readily have been considered as one of resistant rickets. Her history and physical findings did not suggest the presence of renal disease, and urologic findings did not indicate renal damage, anomaly or dysfunction. The usual clinical evidences of acidosis were not manifest. Only through recognition of the lowered alkali reserve and serum chloride content

would one become aware that serious disturbance of electrolyte metabolism was present and predicate that dysfunction of the renal tubules was causative of or contributory to the patient's condition.

To permit accurate appraisal of her condition, the patient was observed in the metabolism ward, and the usual quantitative regimen of diet and collection of excreta was followed. She was given a good diet which included a quart of milk daily, but initially with no added vitamin D. Data relating to retention are shown in table 2 (Jan. 24 to 29, 1933). She retained calcium and phosphorus in small amounts, though much smaller than would be expected for a normal child with the same intake.[3a] The urinary excretion of calcium was not lowered, as often is observed in rickets; neither was it above normal, as might have been expected with

Fig. 2.—Serial roentgenograms of the wrist of patient illustrated in fig. 1: (*A*) at time of initial observation (active rickets); (*B*) two months later, after initial treatment with sodium bicarbonate: healing in progress; (*C*) seven months after initial observation (rickets completely healed; biochemical anomalies controlled through 3 drachms [11.65 Gm.] of sodium bicarbonate daily); (*D*) after three years of alkali therapy (healing of rickets maintained with normal osseous development).

chronic acidosis. The urinary excretion of phosphorus did not exceed the normal (table 2).

On the basis of the biochemical findings it was postulated that the acidosis and ultimately the changes in the bones were the result of loss of fixed base from

3a. Wang, C. C.; Kaucher, M., and Wing, M.: Metabolism of Adolescent Girls: Mineral Metabolism, Am. J. Dis. Child. **52**:41 (July) 1936.

TABLE 1.—*Data Concerning Chemical Constituents of the Blood* and Correlated Factors in a Child with Late Rickets and Acidosis*

Date	Serum: Calcium, Mg.	Serum: Inorganic Phosphorus, Mg.	Serum: Phosphatase, Jenner-Kay Units	Serum: Alk. Res., CO_2, Vols. per Cent	Serum: Cholesterol, Mg.	Whole Blood: Sodium Chloride, Mg.	Whole Blood: Nonprotein Nitrogen, Mg.	Cell Volume, per Cent	Corpuscle Ester Phosphorus, Mg.	Other Blood Findings	Roentgenologic Report	Diet and Medication
1933												
1/20	10.6	3.0	71.5	..	185	...	..	43	45	.....	.....	High Ca diet
1/27	10.6	3.1	54.5	28	185	250	47	43	50	Plasma protein 7.3 Gm. Plasma albumin 5.0 Gm. Uric acid 4 mg. Urea nitrogen 9.8 mg.	Generalized decrease in Ca content; definite evidence of late rickets	Low Ca diet; cod liver oil 3 tsp. daily
1/30	10.3	2.4	46	..	...	...	49	..	..	.....	.....	High Ca diet 2/1; medication as from 1/27; sodium bicarbonate, 1½ tsp. daily and cod liver oil; regimen continued
1/31	....	2.8	59	32	...	270	44					
2/20	11.0	3.1	81.3	28	...	430	..	41				
3/ 7	10.6	3.6	57.5	50	...	420	..	45	55	.....	Continued evidence of rickets	
3/22	11.5	4.6	81.8									
3/28	10.8	5.3	84.4	35†	...	...	..	42	58	.....	Continued evidence of rickets; Ca content subnormal	
3/30	10.5	4.5	80.1	36†	...	...	..	40	60	.....	.....	Sodium bicarbonate, 3 tsp. daily and cod liver oil; regimen continued indefinitely
4/21	10.6	5.6	72.6	35†	...	...	..	44	65			
5/22	10.9	5.2	32.4	58‡	...	...	..	40	65	.....	Continued evidence of rickets; Ca content slightly subnormal; rachitic process apparently healing	
8/ 1	11.5	5.5	36.2	54‡	...	...	..	42	..	....	Ca content normal; excellent healing and deposition of Ca	
1935												
12/ 4	10.2	2.8	....	..	...	...	..	..	..	.....	.....	Sodium bicarbonate
12/16	10.6	3.1	17.1	21	300	613§	48	..	..	.....	No evidence of rickets	No therapy; high Ca diet
12/21	....	...	....	28	...	...	..	..	..	.....	.....	Pitressin 1 cc. daily; 12/23, pitressin 5 cc.
12/24	....	...	....	29	...	...	..	..	..	.....	.....	12/29 to 1/3, sodium and potassium citrates 10 Gm. daily; 12/30, pitressin 5 cc.; 12/31, pitressin 1 cc.
1936												
1/ 3	....	...	....	48	...	...	..	..	..	Urea clearance 52% normal; creatinine 1.1 mg.; uric acid 2.7 mg.; serum sodium 353 mg.	.....	1/3 to 1/6, sodium and potassium citrates 5 Gm. daily; 200 mg. posterior pituitary powder daily; 1/6 to 1/11, 4 to 7 grains (0.26 to 0.45 Gm.) thyroid daily
1/11	9.6	2.2	....	41	...	622§						
1/12‖	...	...	....	40	...	...	..	..	..	Serum sodium 347 mg.		

* Values in terms of 100 cc. of blood or serum.
† Before the ingestion of sodium bicarbonate.
‡ After the ingestion of sodium bicarbonate.
§ Serum.
‖ Post mortem.

the body, even though the underlying cause for such loss was not clear. A regimen was prescribed based on the ingestion of a complete diet including each day a quart of milk and 3 teaspoonfuls of cod liver oil, with administration of ½ teaspoonful of sodium bicarbonate three times daily (6.8 Gm. daily).

During this first stay in the hospital, before therapy was instituted, the patient had one of her "attacks of weakness." She wakened at 2 a. m. complaining of muscular soreness and stiffness. The difficulty increased until by 5 a. m. she was unable to move voluntarily. At 6 a. m., four hours after the attack began, the left side of the body was again normal, and the right side showed improvement. The patient was still unable to stand. A few hours later she had recovered and appeared perfectly well.

She was sent home with the prescribed regimen of good diet, vitamin D and sodium bicarbonate and was instructed to return at intervals to the outpatient department. The chloride content of the serum was approximately normal at the first examination, three weeks after therapy had been instituted; the inorganic phosphorus level rose very slowly, although the increase in corpuscle ester phosphorus indicated that healing of the rickets was in progress (table 1). The patient was again hospitalized after two months of the given regimen. Although the rickets was found to be still active, the observed results of therapy exceeded expectations. The weakness and difficulty in locomotion had disappeared. The patient walked and exercised without hindrance and stated that she felt better than she had for years. She had grown an inch in height. Her first menstrual period occurred during this period of hospitalization. Roentgenograms showed that the rickets was in process of healing and that the density of the cortex had increased (fig. 2*b*); albuminuria no longer was demonstrable, but the polyuria, fixed low specific gravity and neutrality of the urine persisted. When sodium bicarbonate was given, the alkali reserve was normal, but when administration of sodium bicarbonate was omitted prior to the drawing of blood, the alkali reserve of fasting blood was as low as had been noted initially. The phosphatase level was still distinctly above normal.

Studies of retention showed that the child was retaining ample amounts of calcium, phosphorus and fixed base other than calcium (table 2, March 26 to 29, 1933). The urinary excretion of calcium was only one third of its former level; the urinary excretion of phosphorus was unchanged. Abrupt lowering of the urinary excretion of calcium together with daily retention of large amounts of this element is often observed during rapid deposition of bone mineral after serious depletion,[4] and in this patient it may be regarded as proof that the calcium reserve of the bones was no longer needed to supply fixed base. Nevertheless, because of the persistence of hypophosphatemia the dose of sodium bicarbonate was doubled, so that subsequently the patient received 3 teaspoonfuls daily.

The child was seen in the outclinic at intervals. Studies of the blood and roentgen examinations indicated that healing was progressive. Seven months after the initial observation she was clinically well; most of the deformity of the legs had corrected itself spontaneously, and roentgenograms showed complete healing of the rickets (fig. 2*C*). The polyuria and the neutrality and low fixed specific gravity of the urine still were manifest. The inorganic phosphorus content of the serum was normal. The ester phosphorus of the corpuscles was above the average value for a child of her age. The phosphatase had decreased noticeably but still was about twice the normal value, as often is observed in late rickets when healing is newly complete.

4. Boyd, J. D.; Milgram, J. E., and Stearns, G.: Clinical Hyperparathyroidism, J. A. M. A. **93**:684 (Aug. 31) 1929.

The patient continued on the prescribed regimen for a total period of three years. During that time she grew to apparently normal physical maturity and was active and happy and free from symptoms other than occasional attacks of peripheral weakness. One such attack occurred in November 1935. In December of that year she was brought to the outpatient department of the hospital. The calcium content of the serum was found to be normal, but the inorganic phosphorus content had decreased to 2.8 mg. per hundred cubic centimeters. The record does not reveal whether alkali therapy had been lax while she was at home. The child was hospitalized on December 16 for further study. She was then 60½ inches (153.7 cm.) tall and weighed 127 pounds (57.7 Kg.). Neither rickets nor osteoporosis was evident roentgenographically despite the low content of inorganic phosphorus in the serum (fig. 2*d*). The phosphatase level was not elevated.

TABLE 2.—*Excretion and Retention of Calcium, Total Fixed Base, Phosphorus and Nitrogen by Subject with Late Rickets*

Date	Intake	Urine	Feces	Retention	Medication
		Calcium (Milliequivalents in 24 Hours)			
1/24-29/33*	73	7	59	+ 7	None
3/26-31/33	76	2	24	50	Sodium bicarbonate and cod liver oil
12/18-23/35	92	13	72	6	None
		Total Fixed Base † (Milliequivalents in 24 Hours)			
1/24-29/33	205	159	60	—14	None
3/26-31/33	304	199	33	72	Sodium bicarbonate and cod liver oil
12/18-23/35	...	228‡	..	..	None
		Phosphorus § (Milliequivalents in 24 Hours)			
1/24-29/33	69	40	30	— 2	None
3/26-31/33	71	38	9	22	Sodium bicarbonate and cod liver oil
12/18-23/35	99	43	44	12	None
		Nitrogen (Grams in 24 Hours)			
1/24-29/33	8.49	7.30	0.61	0.58	None
3/26-31/33	8.49	8.65	0.89	—0.95	Sodium bicarbonate and cod liver oil
12/18-23/35	13.00	10.31	1.02	1.67	None

* Rickets active 1/24; healing 3/26; bone normal 12/19/35.
† Not including loss through skin.
‡ Data for two days only.
§ The combining value of phosphorus has been taken as 18/31.

Minimal evidences of deformity of the knees remained, and physical activity seemed unimpaired (fig. 1*B*). The degree of polyuria had increased, with a daily output varying from 3,000 to 5,400 cc. daily. The specific gravity of the urine was low and fixed; the reaction, neutral. The amount of ammonia excreted was still within normal limits. The nonprotein nitrogen content of the blood had not increased over the previous levels (the maximum ever observed was 49 mg. per hundred cubic centimeters). Urea clearance, however, had decreased to 52 per cent of normal. The serum chloride level was normal, as was the alkali reserve during the maintenance of the prescribed dosage of sodium bicarbonate. With omission of sodium bicarbonate therapy, the alkali reserve fell within a few days to half or less of the normal value. The basal metabolic rate was within the lower limit of normality.

All therapy was omitted during a study of retention. The retention of calcium and phosphorus was only fair, similar to that of the first study. The calcium in the urine was nearly double its original value, whereas the intake had increased only about 20 per cent (table 2). When the degree of excretion of calcium in

the urine is compared with that of normal girls of the same age and intake, however, the values cannot be considered unusual. The excretion of ammonia nitrogen in the urine was 277 mg. daily, an amount expected of a normal child, but not the increased excretion expected under conditions calling for conservation of fixed base. Excretion of organic acid in the urine was not inordinately high, in no degree sufficient to account for the evident drain of base from the body.

Fig. 3.—Photomicrograph of renal tubules, showing minimal degree of pathologic change noted post mortem, in contrast with the clinical and laboratory evidences of disturbed tubular function. The glomeruli were free from evidences of pathologic change.

To determine whether pituitary dysfunction was instrumental in maintaining the polyuria, the patient was given posterior pituitary extract for several days, during which interval administration of alkali again was discontinued. No effect

on the volume or the concentration of the urine was noted. The child was sent home on December 24, to return December 28. During her stay at home she suffered from a severe attack of weakness. Alkali therapy, 10 Gm. of mixed sodium and potassium citrates daily, was instituted on December 29. On January 3 the dose was cut in half. During the period of ingestion of citrate the urinary calcium decreased by about 20 per cent; the organic acid titer was practically unchanged. Thyroid therapy was then tried for a week, during which time a total of 34 grains (2.2 Gm.) was given without demonstrable effect on the constituents of the blood or urine. The serum sodium at this time was of normal value.

In the course of this last period of hospitalization the patient had two attacks of weakness and paresthesia, similar to the one observed during her first period of hospitalization. The first of these, which occurred a day before the completion of observation, was more severe than any experienced previously. A few hours afterward she had another, which terminated in death in collapse, preceded by gasping respiration.

A necropsy within three hours of the time of death offered no explanation of the immediate cause of death or of the underlying difficulty. Minor changes were noted in the kidneys, but no more than those frequently seen which are unrelated to dysfunction (fig. 3). The adrenal glands, ovaries and parathyroids were normal throughout. The liver appeared normal, grossly and microscopically. The pituitary gland and brain were not examined. There were evidences of moderate chronic thyroiditis, but seemingly enough normal-appearing thyroid substance was present to provide for proper function; no adenomatous tissue was noted. Blood drawn from the heart immediately post mortem had an alkali reserve of 40 volumes per cent and a normal content of sodium.[5]

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5. Doctor E. D. Warner, of the department of pathology, reviewed the histopathologic appearance of the kidneys and of the thyroid gland. The following is quoted from his report:

"Kidneys: The parenchyma and architecture are for the most part well preserved except for a few small scars which contain hyalinized glomerular remnants and atrophic tubules. Some pressure atrophy is evident in the walls of the simple cysts described in gross. The convoluted tubules are considerably dilated throughout and contain granular debris. The epithelium, however, is well preserved and shows only very mild vacuolation. The glomerular structures are essentially normal except for the scattered scars. The arterial walls are within normal limits. There are a few small areas of calcium deposition in the pyramids near the pelvis. An apparently incidental finding is the presence of multiple small foci of papillary overgrowth of tubular epithelium forming tiny adenoma-like structures. The pelvic mucosa is intact, and there is only very minimal lymphocytic infiltration.

"Thyroid: There is rather marked infiltration of the stroma with lymphocytes, with definite follicle formation in places. There is moderate increase in fibrous connective tissue, with considerable disruption of normal architecture. Many of the acini are atrophic, while others are quite dilated. Foci of hyperplastic acini are also present. The histologic appearance is that of a rather mild degree of chronic thyroiditis with some irregular involutional changes."

COMMENT

This patient's inability to conserve base seemed dependent on the persistent excretion of a large volume of nonacid urine. Apparently she could not excrete urine with a p_H more acid than that of blood. The normal person conserves base through several mechanisms, most important of which are the excretion of acid phosphates and the substitution of ammonium ions for equivalent amounts of base. Conservation of fluid also plays a role in this process. Our subject could not conserve water, and she did not excrete ammonium ions in amounts sufficient to meet her need for conservation of base. In the normal subject, increased formation of ammonia becomes apparent as urine reaches its maximum level of acidity, but the increased level of excretion is maintained for some time after the demand for increased elimination of acid has ceased.[6] Evidence was not found in the literature as to whether any marked increase in the formation of ammonia can arise concomitant with the excretion of nonacid urine. Our patient's failure to excrete larger amounts of ammonia may be attributable to perversion of her whole pattern of electrolyte and water control, rather than to primary derangement of function of the renal tubules.

The findings in the blood and urine of this child resemble those obtained experimentally in dogs by Hendrix and Calvin.[7] They found that for twenty-four hours or longer after the injection of neutral salts or of urea the resultant diuresis was accompanied by an excessive loss of base through the kidney, followed by pronounced lowering of the alkali reserve of the blood. These changes occurred within a few hours and were ascribed to lack of reabsorption of base through renal tubules which were overtaxed by the diuresis. It should be emphasized that the reported studies represented relatively brief periods of induced abnormality and in that regard the results might differ considerably from those to be expected if diuresis were to persist for years without interruption. It is conceivable, however, that formation of ammonia may be depressed through rapid passage of fluid through the tubules. Although such an explanation is attractive in the case of our patient, study of the composition of the urine (table 3) fails to demonstrate excessive excretion of any single neutral salt or of urea.

A recent study of the Harrisons [7a] showed that in dogs which were maintained in chronic acidosis by feeding ammonium chloride, the rate

6. Gamble, J. L.; Ross, G. S., and Tisdall, F. F.: The Metabolism of Fixed Base During Fasting, J. Biol. Chem. **57**:633, 1923.

7. Hendrix, B. M., and Calvin, D. B.: The Loss of Bases in Diuresis and Its Effect upon the Alkali Reserve of the Blood, J. Biol. Chem. **65**:197, 1925.

7a. Harrison, H. E., and Harrison, H. C.: The Effect of Acidosis upon the Renal Tubular Reabsorption of Phosphate, Am. J. Physiol. **134**:781 (Nov.) 1941.

of reabsorption of phosphate by the renal tubules was decreased. The amount of decrease was related both to the severity of the acidosis and to its duration and was sufficient to account for the observed decrease in plasma phosphate. These findings seem particularly relevant to the study of our patient, who had both chronic acidosis and rickets with hypophosphatemia. If a decreased rate of reabsorption of phosphorus through the renal tubules were primarily responsible for the development of rickets in this child, one would expect to observe an increased reabsorption, with resultant decrease of phosphorus in the urine on healing of the rickets. In late January 1933, before therapy was begun,

TABLE 3.—*Acid-Base Relationships of Urine of Subject with Late Rickets (Milliequivalents Excreted in Twenty-Four Hours)*

			Cations						Anions				
Date and Treatment	Average Urine Volume, Cc. per 24 Hr.	Specific Gravity × 1,000	Calcium	Sodium	Potassium	Total Fixed Base	Ammonia	Titratable Acid	Chlorine	Inorganic Phosphorus	Inorganic Sulfur	Organic Acid	pH *
1/24-29/33	2,425	10 to 12	7	...	..	159	..	..	97	40	26	..	...
3/26-31/33, sodium bicarbonate and cod liver oil.....	2,200	.....	2	146	62	199	8	3.6	88	38	28	..	...
12/19-26/35, no alkali....	3,380	2 to 5	13	112	63	228†	16	..	118	43	..	51	7.4
1/2-7/36, sodium and potassium citrate.....	3,700	1 to 4	11	150	44	265	10	10	132	52	..	43	8.0

* Approximate; measured colorimetrically for each specimen as voided.
† Determined for first two days only.

the acidosis was severe and the serum inorganic phosphorus varied from 3.1 to 2.4 mg. for each 100 cc. (table 1). During this study the child excreted an average of 40 milliequivalents (712 mg.) of phosphorus during twenty-four hours (table 2), with an intake of 69 milliequivalents (1,192 mg.). In late March of the same year, with an intake of 71 milliequivalents (1,212 mg.), the urinary phosphorus was still 38 milliequivalents (684 mg.). The serum inorganic phosphorus had risen sharply, varying from 4.5 to 5.3 mg. for each 100 cc., and roentgenologic studies showed that healing of the rickets had begun. The acidosis was only in part compensated. Therefore, it seems improbable that the amount of reabsorption of phosphate through the urinary tubules was

the primary factor involved in the healing of rickets in this patient. From the clinical and biochemical findings it appears more probable that the factor which led to the development of rachitic lesions was the inability to conserve base. The gradual but unremittent drain of base from her body led to the depletion of mineral in the bones and to the chronic acidosis and lowered chloride content of the serum which were noted initially. Administration of excess cation as sodium bicarbonate permitted retention of calcium, and healing was initiated even before the alkali reserve had been restored to normal levels. In one of the patients previously reported on [2a] a similar observation was made; healing progressed with a dosage of alkali which was insufficient to correct completely the lowered alkali reserve.

Vitamin D and other dietary therapy undoubtedly contributed to the healing of this patient's rickets, once the deficit of base had been corrected. We do not feel that healing could have resulted through improvement of the diet alone. In the other patient cited in the preceding paragraph [2a] some degree of healing was noted after six months' observation under dietary therapy without administration of alkali; further healing did not occur until regular alkali medication was commenced. To expect complete recovery in all respects in patients similar to these through vitamin D therapy alone would imply that the complete syndrome is explainable on the basis of a deficiency of that vitamin.

The effectiveness of vitamin D in this patient would probably depend on increased reabsorption of phosphate through the renal tubules,[7b] thus heightening the effect produced by correction of the acidosis. Vitamin D was given to the child at the same time alkali therapy was instituted; their combined effect on urinary phosphorus excretion seems insufficient to account for the degree of healing observed. The peculiar attacks of weakness experienced by this child may have been related to her disturbed electrolyte equilibrium. In some regards they resembled those seen with tetany or with adrenal insufficiency. The absence of detectable lesions in the adrenal or the parathyroid glands speaks against their dysfunction; moreover, the freedom from hypocalcemia or from lowering of the serum sodium level makes such endocrine disturbance unlikely.

De Toni and Fanconi have described a syndrome which includes many of the conditions observed in the patient reported on here.[8]

7b. Harrison, H. E., and Harrison, H. C.: The Renal Excretion of Inorganic Phosphate in Relation to the Action of Vitamin D and Parathyroid Hormone, J. Clin. Investigation **20**:47 (Jan.) 1941.

8. de Toni, G.: Remarks on Relationship Between Renal Rickets (Renal Dwarfism) and Renal Diabetes, Acta pædiat. **16**:479, 1933. Fanconi, G.: Der frühinfantile nephrotisch-glykosurische Zwergwuchs mit hypophosphatämischer Rachitis, Jahrb. f. Kinderh. **147**:299, 1936.

Certain features distinguish her condition from that syndrome. Our patient was free from evidence of disorder until midchildhood; she was not dwarfed; she was aglycosuric, and she remained free from albuminuria once alkali therapy was established. She did not suffer from inability to regulate body temperature but did have the peculiar attacks of weakness mentioned. The elements common to our patient's condition and the de Toni-Fanconi syndrome, including polyuria, low and fixed specific gravity of the urine and acidosis (which some of these patients present) lead one to speculate that the de Toni-Fanconi syndrome is but part of a deep-seated metabolic syndrome which may be manifested in several ways. The common factor is the chronic disturbance of electrolyte metabolism associated with disturbed mineralization of bone. The functional disorder of the renal tubules in our patient without evidence of damage to these structures (fig. 3) may perhaps be considered as evidence that the fundamental disturbance giving rise to the entire syndrome was not in the kidney but in some of the other regulatory tissues, perhaps a lesion of the diencephalon, or of some other division of the autonomic system. The literature contains several reports indicating that disturbances of mineral metabolism may arise from such lesions.[9] Because permission was not granted for necropsy of the central nervous system, the existence of such lesions could not be determined in our patient.

The history of this subject shows that although the fundamental disorder was not cured, the healing of rickets, spontaneous correction of bony deformities and resumption of growth enabled her to live a nearly normal life for three years. This record and that of the other patient previously reported on [2a, b] serve to emphasive the secondary nature of the rachitic lesions and the value of base therapy in the control of rickets associated with chronic acidosis. Even though such therapy may not alter the ultimate outcome, suitable administration of base may lead to a state of improved health, lessened incapacity and prolonged life expectancy.

SUMMARY

The dependence of late rickets associated with chronic acidosis on deficiency of base and its cure through base therapy are illustrated by

9. Chown, B., and Lee, M.: Renal Rickets and Dwarfism as Pituitary Disease, Am. J. Dis. Child. **53**:117 (Jan., pt. 1) 1937. Berg, B. N.; Hess, A. F., and Sherman, E.: Changes in Percentages of Calcium and Phosphorus of Blood Following Section of Sympathetic and Vagus Nerves, J. Exper. Med. **47**:105 (Jan.) 1928; Alterations in Calcium Level of Blood Following Section of Spinal Cord, ibid. **47**:115 (Jan.) 1928. Fanconi, G.: Contributo alla pathologia del metabolismo del metabolismo del cloruro di sodio (Il diabete insipido oculto), Riv. di clin. pediat. **36**:708 (Aug.) 1938.

clinical and metabolic observations on a patient with severe base deficit of unknown origin. The presence of severe dysfunction of the renal tubules without damage to cell structure leads to the conclusion that the fundamental cause of the disorder was extrarenal. The results of urinalysis were interpreted as not supporting the theory that rickets associated with chronic acidosis results solely from decreased reabsorption of phosphate by the renal tubules. Evidence is offered as to the value of alkali therapy in chronic acidosis for the prevention or cure of associated rickets.

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PERTUSSIS ANTIBODIES IN PREGNANT WOMEN

PROTECTIVE, AGGLUTINATING AND COMPLEMENT-FIXING ANTIBODIES BEFORE AND AFTER VACCINATION

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It was reported previously [1a, b] that pertussis-protective antibodies were found in a large percentage of patients who whooped three weeks or longer, that these antibodies were seldom found earlier in the disease and that they were present in all patients who had recently recovered from pertussis. Agglutinins were found in less than one half of the patients who were tested during the infection and in only a small percentage of those tested after recovery. Complement-fixing antibodies were found in some of the patients during the infection but not after recovery. The results obtained in these studies showed that the development of protective antibodies seemed to parallel the development of immunity during convalescence or after recovery and that the presence of these antibodies may be taken as presumptive evidence of immunity to pertussis. Since agglutinins and complement-fixing antibodies were seldom found during convalescence or after recovery and when they were present their titers did not correspond either to the duration of the illness

From the Bureau of Laboratories, New York City Department of Health.

1. (*a*) Mishulow, L.; Klein, I. F.; Liss, M. M., and Leifer, L.: Protection of Mice Against H. Pertussis by Serum, J. Immunol. **37**:17-32 (July) 1939. (*b*) Mishulow, L.; Siegel, M.; Leifer, L., and Berkey, S. R.: A Study of Pertussis Antibodies: Protective, Agglutinating and Complement-Fixing Antibodies in Patients with Pertussis, Persons Exposed to Pertussis and Persons with No Known Exposure, Am. J. Dis. Child. **63**:875-890 (May) 1942. (*c*) Mishulow, L.; Wilkes, E. T.; Liss, M. M.; Lewis, E.; Berkey, S. R., and Leifer, L.: Stimulation of Pertussis-Protective Antibodies by Vaccination: A Comparative Study of Protective, Agglutinating and Complement-Fixing Antibodies, ibid. **62**:1205-1216 (Dec.) 1941.

or to the protective power of the serums, their presence cannot be relied on to determine immunity to this disease.

Protective antibodies were found in more than half of the persons who were intimately exposed to active pertussis, although none of them showed the typical symptoms of the disease and some of them showed no symptoms of illness after exposure. Agglutinins and complement-fixing antibodies were present in approximately the same percentage of persons in this group as of those with active pertussis.

Evidence was presented that development of these antibodies was not stimulated by other infections of the respiratory tract. Judging by the presence of protective antibodies, one may assume that immunity to pertussis is stimulated in many persons by exposure to active pertussis even when the typical symptoms of the disease do not develop.

It was also reported [1c] that infants and children under 4 years of age who had no pertussis infection or previous vaccination against this disease had no protective, agglutinating or complement-fixing antibodies; that 15.2 per cent of older children and adults with a similar history had protective antibodies [1b] and 5.5 per cent of these had agglutinins but none of them had any complement-fixing antibodies. The presence of the antibodies in the older children and adults could not be attributed to immunity to this disease which is acquired with age, since persons with and without these antibodies were found in all the age groups tested. In view of the fact that the production of pertussis-protective antibodies was stimulated in a large percentage of persons who showed no typical symptoms after they were exposed to active pertussis, the presence of these antibodies in persons without a history of pertussis was attributed to subclinical or mild atypical pertussis infections due to unknown exposures.

These results seemed to us significant, because they help to explain why infants and young children are as a rule susceptible to pertussis from the day of birth, and they suggest the reason for the resistance of some older children and adults when they are exposed to active pertussis.

It was found in studies of the immunologic response to pertussis vaccination [1c] that development of protective, agglutinating and complement-fixing antibodies was stimulated in children 2 years 3 months to 5 years 10 months of age within one month after vaccination with 50,000,000,000 to 90,000,000,000 bacilli of our pertussis toxin-vaccine; that the maximum titers of protective antibodies were obtained between one and two months after vaccination, and that these antibodies were still present in 6 children who were tested one and a half, three and

four years respectively after vaccination. Thus the response to vaccination was rapid and apparently lasting, although the number of children tested at that time was too small to justify the drawing of definite conclusions.

The present investigation was carried out to determine whether pertussis-protective, agglutinating and complement-fixing antibodies are present in a significant percentage of women of child-bearing age, many of whom have had chances to be exposed to pertussis either in their own families or among their neighbors who have children, and to determine how they would respond to immunization if the vaccination were carried out during pregnancy. A group of 29 women, 19 to 37 years of age, was selected for this study. All of them were in the third trimester of pregnancy, and none of them had been previously immunized against pertussis. Three of them gave a history of pertussis in childhood; 15 had probably had pertussis in childhood, and 11 had not had it. These studies were carried out as follows:

After preimmunization bleedings were taken, the women were given a series of injections of our pertussis toxin-vaccine,[2] which contained 10,000,000,000 bacilli per cubic centimeter. The injections were made at two week intervals, the dose beginning with 10,000,000,000 bacilli and being increased until 90,000,000,000 to 150,000,000,000 bacilli were given. No severe reaction or untoward results occurred in any of the patients because of the vaccination.[3]

After vaccination was completed, bleedings were taken at the time of delivery. We had planned to complete the vaccinations six to eight weeks before delivery in order to allow a sufficient period for the stimulation of protective antibodies, since we had found previously that the maximum titer of protective antibodies was obtained between one and two months after vaccination.[1e] But delivery took place in some instances much sooner than was expected; therefore, about one third of the vaccinated women were tested one to three and a half weeks after vaccination. The remaining subjects were tested four to ten weeks after vaccination.

The prevaccination and postvaccination bleedings were tested for pertussis-protective, agglutinating and complement-fixing antibodies. Both bleedings were tested at the same time in order to rule out any possible variation in technic or any difference in the susceptibility of different lots of mice used for the tests.

The question arose whether the physical condition of the women at the time of delivery would cause nonspecific positive reactions. Therefore, bleedings were obtained on the day of delivery from 3 unvaccinated women who had no history

2. For the preparation of this vaccine see Mishulow and others.[1e]

3. These studies were made in conjunction with Drs. Philip Cohen and Samuel Scadron, who studied placental transmission of pertussis antibodies from the mother to the newborn child (Cohen, P., and Scadron, S.: Placental Transmission of Pertussis Antibodies, to be published). The vaccinations ware carried out by them at the Jewish Maternal Clinic of the Beth Israel Hospital, New York, and the same persons were tested in both investigations.

of pertussis, and their serums were tested in the same manner as the others. Our methods of testing for protective, agglutinating and complement-fixing antibodies against pertussis have been described in detail in previous publications.[1]

In the tests for protective antibodies groups of mice were given intramuscular injections of 0.2 cc. of the serum nineteen to twenty hours previous to the intraperitoneal injection of a multiple killing dose of virulent pertussis organisms suspended in 1 cc. of a 4 per cent mucin solution. At each test similar groups of mice were given injections of a known positive serum and of the test doses of the culture without serum; these served as controls of the validity of the test (tables 1 and 2). The serum was considered positive for protective antibodies when 30 per cent or more of the mice survived seven to eight days. All mice that died during the period of observation were examined for the presence of another infec-

TABLE 1.—*Virulence of the Culture of Haemophilus Pertussis During the Period of This Investigation*

Dose, Millions of Organisms	Number of Mice Which Died in				Period of Illness, Days
	Test 1	Test 2	Test 3	Test 4	
500*	10/10	10/10	10/10	9/9	2 to 3
250*	9/10	10/10	10/10	8/8	3 to 6
125	7/9	4/5	6/10	8/10	5 to 8
62.5	6/11	4/5	3/9	3/4	5 to 8
31.2	0/10	1/5	1/9	3/5	5 to 8

* The dose used in testing for protective antibodies.

TABLE 2.—*Number of Mice Protected in Each Test with Control Positive Serum*
(Period of Test, 7 to 8 Days)

	Test 1	Test 2	Test 3	Test 4
Survived	9/9	8/10	9/9	8/9
Percentage protected	100	80	100	88.8

tion; if one was found, the mouse was eliminated. The blood of all mice that had had injections of the culture of Haemophilus pertussis without serum was examined after the animals' death, and H. pertussis was usually recovered from the heart's blood in the first four days of the test unless the plates were contaminated by other organisms that invaded the blood post mortem when the mice died during the night.

The results of tests for agglutination were recorded in terms of the highest dilution of the serum that showed distinctly visible clumps. Indistinct or no agglutination in a 1:10 dilution of the serum was recorded as negative. Complement fixation was recorded in terms of the smallest amount of serum that gave complete fixation under standard conditions.[1c] Incomplete or no fixation in 0.02 cc. of the serum was recorded as negative.

The results obtained in this investigation are given in tables 1, 2 and 3.

TABLE 3.—*Protective, Agglutinating and Complement-Fixing Antibodies in Pregnant Women Before and After Pertussis Vaccination*

Vaccine Dose, Millions of Organisms	Laboratory Number	Age, Yr.	Pertussis in Childhood	Serum Tested *	Result: Agglutination	Result: C. F.	Result: Mouse Protection: Number Survived	Result: Mouse Protection: Per Cent
90,000	C-12	33	No	Before vaccination	0	0	0/10	0
				1 week after vaccination	950	0	7/9	77.7
	C-1	30	Probably	Before vaccination	0	0	0/9	0
				1½ weeks after vaccination	350	0.009	8/10	80
120,000	C-19	26	Probably	Before vaccination	75	0.02	4/10	40
				1 week after vaccination	300	0.007	10/10	100
	C-31	25	Probably	Before vaccination	0	0	1/9	0
				2 weeks after vaccination	900	0.02	10/10	100
	C-15	30	No	Before vaccination	0	0	10/10	100
				2½ weeks after vaccination	350	0.02	10/10	100
	C-20	37	Probably	Before vaccination	0	0.005	0/10	0
				4 weeks after vaccination	30	0.004	8/9	88.8
	C-40	36	Probably	Before vaccination	0	0	0/10	0
				4 weeks after vaccination	25	0	8/8	100
	C-42	26	Probably	Before vaccination	0	0	0/10	0
				4 weeks after vaccination	25	0	6/10	60
	C-9	29	No	Before vaccination	0	0	1/10	0
				4 weeks after vaccination	25	0.02	9/9	100
	C-26	19	No	Before vaccination	50	0	0/9	0
				5 weeks after vaccination	600	0.02	7/8	87.5
	C-39	33	Probably	Before vaccination	0	0	4/9	44.4
				10 weeks after vaccination	800	0.02	10/10	100
150,000	C-2	27	Probably	Before vaccination	25	0	3/6	50
				2 weeks after vaccination	650	0.009	8/9	88.8
	C-33	22	Yes	Before vaccination	50	0	5/9	55.5
				3 weeks after vaccination	900	0.02	9/10	90
	C-32	29	No	Before vaccination	0	0	4/7	57
				3½ weeks after vaccination	600	0.006	10/10	100
	C-37	23	Probably	Before vaccination	0	0	0/8	0
				3½ weeks after vaccination	200	0	8/10	80
	C-38	22	No	Before vaccination	0	0	1/10	0
				4 weeks after vaccination	200	0.02	8/8	100
	C-30	22	Probably	Before vaccination	0	0	1/9	0
				4 weeks after vaccination	900	0.007	7/9	77.7
	C-21	24	Probably	Before vaccination	0	0	2/9	?
				4½ weeks after vaccination	250	0.02	8/8	100
	C-5	23	No	Before vaccination	0	0	2/10	?
				5 weeks after vaccination	150	0	8/8	100
	C-18	24	Yes	Before vaccination	0	0	9/10	90
				5 weeks after vaccination	700	0.007	8/9	88.8
	C-25	19	Yes	Before vaccination	0	0	0/6	0
				5 weeks after vaccination	450	0.01	3/8	37.5
	C-34	32	No	Before vaccination	0	0	7/10	70
				5 weeks after vaccination	800	0.006	6/7	85.5
	C-36	22	Probably	Before vaccination	0	0	3/9	33.3
				6 weeks after vaccination	25	<0.01	7/9	77.7
	C-14	26	No	Before vaccination	0	0	0/6	0
				6 weeks after vaccination	75	0	6/9	66.6
	C-6	24	No	Before vaccination	0	0	1/8	0
				6½ weeks after vaccination	75	0.009	8/10	80
	C-35	31	Probably	Before vaccination	0	0	6/9	66.6
				7 weeks after vaccination	300	0.01	9/10	90
	C 3	32	No	Before vaccination	0	0	0/8	0
				7½ weeks after vaccination	0	0.02	6/10	60
	C-41	32	Probably	Before vaccination	0	0	0/9	0
				8½ † weeks after vaccination	25	0.02	7/10	70
	C-43	30	Probably	Before vaccination	0	0	1/9	0
				9 † weeks after vaccination	25	0	4/10	40
0	C-62	22	No	On day of delivery	0	0	1/8	0
	C-63	22	No	On day of delivery	0	0	0/8	0
	C-64	19	No	On day of delivery	0	0	0/10	0

Before vaccination, 29 subjects tested during the third trimester of pregnancy
- Protective antibodies in 10 persons..... 34.4%
- Agglutinating antibodies in 4 persons..... 13.7%
- Complement-fixing antibodies in 2 persons..... 6.8%

After vaccination, the same subjects tested on the day of delivery
- Protective antibodies in 29 persons..... 100%
- Agglutinating antibodies in 27 persons..... 93.1%
- Complement-fixing antibodies in 22 persons..... 75.8%

Unvaccinated, 3 control subjects tested on the day of delivery
- Protective antibodies in 0 persons
- Agglutinating antibodies in 0 persons
- Complement-fixing antibodies in 0 persons

Total tested, 32 unvaccinated women
- Protective antibodies in 10 persons..... 31.2%
- Agglutinating antibodies in 4 persons..... 12.5%
- Complement-fixing antibodies in 2 persons..... 6.2%

* The serums after vaccination were taken at time of delivery.
† These 2 women were tested 2 and 2½ weeks respectively after delivery.

COMMENT

The results obtained in this investigation show that 10, or 34.4 per cent, of the 29 women who were tested during pregnancy had pertussis-protective antibodies before vaccination; 4, or 13.7 per cent, had agglutinins, and 2, or 6.8 per cent, had complement-fixing antibodies. In addition, 3 women who had not had pertussis were tested on the day of delivery, and all of them showed complete absence of these antibodies. Thus, of the 32 women tested 31.2 per cent had protective antibodies; 12.5 per cent had agglutinins and 6.2 per cent had complement-fixing antibodies. This is more than twice the percentage of positive results that we obtained from tests of children and adults who were inmates of an institution.[1b] Many of the women in the present study, however, had a positive or probably positive history of pertussis in childhood, whereas all the children and adults in the previous investigation had a negative history of pertussis.

If the results obtained in this investigation are considered in relation to the histories of pertussis in childhood, they were as follows:

Of the 18 women who had had or probably had had the disease, 7, or 38.8 per cent, had protective antibodies; 3, or 16.6 per cent, had agglutinins, and 2, or 11.1 per cent, had complement-fixing antibodies.

Of the 14 women who had not had the disease, 3, or 21.4 per cent had protective antibodies, and 1, or 7.1 per cent, had agglutinins; none of these had any complement-fixing antibodies.

Although the percentage of positive results for persons who had a history of pertussis in childhood was higher than that for persons without such a history, the difference is not sufficiently great to warrant an assumption that the antibodies persisted from childhood infections. Judging by the evidence obtained previously[1b] that the production of protective antibodies is stimulated in a large percentage of persons through exposure to active pertussis in patients without the typical symptoms of this disease and in some persons who showed no symptoms of illness after exposure, the antibodies in these women must have been produced by rather recent mild or atypical pertussis infections that were not recognized as such. This would explain why the percentage of positive results among the women of child-bearing age was much higher than that among the children and adults in an institution. These women had a much greater chance to be exposed to pertussis, either in their own families or among their neighbors, than the inmates of the institution, who were guarded against exposure to known pertussis.

The antibody response to vaccination was as good in the pregnant women as in the young children that we studied previously. Protective antibodies were present in 100 per cent of them, agglutinins in 93.1 per cent and complement-fixing antibodies in 75.8 per cent, one to ten weeks after vaccination. Three women who had none of the three

types of antibodies before vaccination had protective and agglutinating antibodies one to two weeks after vaccination, and 2 of them also had complement-fixing antibodies.

Of the 29 women who were vaccinated, 10 had protective antibodies before vaccination, and 3 of these 10 also had agglutinins. In addition to these, 1 woman had agglutinins and another had complement-fixing antibodies only. The remaining 17 women had none of these antibodies. If we consider the results that were obtained after vaccination of the 17 women who had no antibodies before vaccination, they were as follows: 17, or 100 per cent, had protective antibodies after vaccination; 16, or 94.1 per cent, had agglutinins, and 10, or 58.8 per cent, had complement-fixing antibodies. Thus pregnancy apparently had no inhibitory effect on the production of antibodies.

The concentration of protective, agglutinating and complement-fixing antibodies seemed to have no direct relation to the dose of the vaccine given, to the time that had elapsed since the completion of vaccination or to the presence of these antibodies before vaccination (table 3), but depended apparently on the person's ability to produce antibodies. We were not able to determine in this study when the antibodies attained their maximum concentration, since the tests were made at irregular intervals and in many instances less than one month after vaccination. We can definitely say, however, that the development of protective, agglutinating and, in most instances, complement-fixing antibodies was stimulated within one month after vaccination. This is in accord with our previous observations.[1c]

That the physical condition of the women at the time of delivery had no influence on the specificity of the tests was shown by the results obtained from the 3 unvaccinated women who were tested on the day of delivery; none of them had any of the three antibodies for which they were tested.

The question of optimum dosage is still under discussion. Good results were reported by various workers with doses from 70,000,000,000 to 140,000,000,000 bacilli (Kendrick and Eldering,[4] Miller and Faber,[5] Sauer,[6] Lapin, Cohen and Weichsel,[7] Silverthorne and Fraser,[8]

4. Kendrick, P., and Eldering, G.: A Study in Active Immunization Against Pertussis, Am. J. Hyg., Sect. B **29**:133-153 (May) 1939.

5. Miller, J. J., Jr., and Faber, H. K.: Immunization Against Pertussis, J. A. M. A. **112**:1145-1148 (March 25) 1939.

6. Sauer, L. W.: Whooping Cough, J. A. M. A. **112**:305-308 (Jan. 28) 1939.

7. Lapin, J. H.; Cohen, P., and Weichsel, M.: Prophylactic Vaccination Against Whooping Cough, Arch. Pediat. **56**:590-598 (Sept.) 1939.

8. Silverthorne, N., and Fraser, D. T.: Whooping Cough, Canad. M. A. J. **38**:556-559 (June) 1938.

Daughtry-Denmark [9] and others). Maclean [10] reported successful vaccination with a total of 16,000,000,000 to 20,000,000,000 bacilli when the first three injections of 4,000,000,000 bacilli each were made at three to seven day intervals and the fourth injection of 4,000,000,000 bacilli was given one month after the third injection. He advised giving an additional injection of 4,000,000,000 bacilli after the immunization course when the child is known to have been exposed. Bell [11] obtained favorable results with 20,000,000,000 alum-precipitated bacilli when they were given in two injections with an interval of four weeks between the injections. Daughtry-Denmark [12] reported equally favorable results in stimulating the production of complement-fixing antibodies with 100,000,000,000 bacilli of pertussis vaccine and with 40,000,000,000 bacilli when the vaccine was alum precipitated. Rambar and others [13] found that the results obtained with a dose of 80,000,000,000 bacilli in stimulating production of bacteriotropins were as good as those with a dose of 100,000,000,000 bacilli.

Small groups of children have been tested with varying doses of vaccine,[14] and it was found that stimulation of the formation of agglutinins was poor when the dose was less than 70,000,000,000 bacilli. Siegel [15] reported no protection clinically with 50,000,000,000 bacilli or less. It has been found in recent studies [1b] that a dose of 90,000,000,000 bacilli stimulated the production of protective, agglutinating and complement-fixing antibodies in young children within one month after vaccination. The present study shows that production of these antibodies is stimulated equally well in adults by doses of 90,000,000,000, 120,000,000,000 and 150,000,000,000 bacilli. The indications are at present that a dose of 90,000,000,000 bacilli for children and 120,000,000,000 bacilli for adults is adequate for prophylactic vaccination.

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9. Daughtry-Denmark, L.: Studies in Whooping Cough, Am. J. Dis. Child. **52**:587-598 (Sept.) 1936.

10. Maclean, I. H.: Prophylactic Inoculation Against Whooping Cough, Proc. Roy. Soc. Med. **33**:425-432 (May) 1940.

11. Bell, J. A.: Pertussis Prophylaxis with Alum Precipitated Vaccine, Pub. Health Rep. **56**:1535-1546 (Aug.) 1941.

12. Daughtry-Denmark, L.: Whooping Cough Vaccine, Am. J. Dis. Child. **63**: 453-466 (March) 1942.

13. Rambar, A. C.; Howell, K.; Denenholz, E. J.; Goldman, M., and Stanard, R.: Studies in Immunity to Pertussis, J. A. M. A. **117**:79-85 (July 12) 1941.

14. Mishulow, L.; Mowry, I., and Orange, R.: A Comparative Study of Agglutinin Response After Pertussis Vaccination with the Sauer Vaccine and with a Toxin-Vaccine and in Untreated Clinical Pertussis, J. Pediat. **9**:492-504 (Oct.) 1936.

15. Siegel, M.: Active Immunization Against Whooping Cough with Various Specific Vaccines, Am. J. Dis. Child. **56**:1294-1303 (Dec.) 1938.

SUMMARY

Twenty-nine women 19 to 37 years of age were tested during the third trimester of pregnancy for pertussis-protective, agglutinating and complement-fixing antibodies before vaccination and on the day of delivery, one to ten weeks after vaccination, with 90,000,000,000 to 150,000,000,000 bacilli of our pertussis toxin-vaccine. None of these women had been previously immunized against pertussis. Three of them gave a history of pertussis in childhood; 15 probably had had pertussis in childhood, and 11 had no history of pertussis.

Before vaccination 10, or 34.4 per cent, of these women had pertussis-protective antibodies. Three of those who had protective antibodies also had agglutinins, and another had agglutinins only (13.7 per cent of the total had agglutinins). One woman had complement-fixing antibodies in addition to protective and agglutinating antibodies and 1 had complement-fixing antibodies only (6.8 per cent of the total had complement-fixing antibodies). Seventeen women of this group had no antibodies.

After vaccination all of the 29 women, or 100 per cent, had protective antibodies; 27, or 93.1 per cent, had agglutinins, and 22, or 75.8 per cent, had complement-fixing antibodies. Of the 17 women who had no pertussis antibodies before vaccination all had protective antibodies after vaccination; 16, or 94.1 per cent, had agglutinins, and 10, or 58.8 per cent, had complement-fixing antibodies.

Three unvaccinated women were tested on the day of delivery in order to determine whether the physical condition on the day of delivery would cause nonspecific positive reactions. The tests of these women elicited negative responses for the three antibodies.

A total of 32 women were tested who had had no recent pertussis infection and no previous vaccination against this disease. Of these 10, or 31.2 per cent, had protective antibodies; 4, or 12.5 per cent, had agglutinins, and 2, or 6.2 per cent, had complement-fixing antibodies.

CONCLUSIONS

If one may judge by the presence of pertussis-protective antibodies, a considerable percentage of women 19 to 37 years of age possess some immunity against pertussis. Of a total of 32 women tested, 31.2 per cent had protective antibodies. The presence of these antibodies is attributed to a fairly recent mild or atypical pertussis infection that was not recognized as such rather than to an infection in childhood.

Women who were vaccinated during pregnancy responded readily to the vaccination. Protective antibodies were present in all of the 29 vaccinated women in one to ten weeks after vaccination, agglutinins were present in 93.1 per cent and complement-fixing antibodies in

75.8 per cent. Of the 17 women in this group who had no pertussis antibodies before vaccination 100 per cent had protective antibodies after vaccination, 94.1 per cent had agglutinins and 58.8 per cent had complement-fixing antibodies.

There were no unduly severe reactions or untoward results from the vaccination in the women who were vaccinated during the third trimester of pregnancy by the method of Cohen and Scadron.[3] Unless there are other contraindications to vaccination, it would seem desirable to vaccinate pregnant women who have no protective antibodies in order to protect them against possible pertussis infection during pregnancy.

A dose of 90,000,000,000 bacilli for children and 120,000,000,000 for adults seems adequate.

Technical assistance in carrying out this investigation was given by Miss Rose Weissman and Mrs. Evelyn A. Luskin.

Bureau of Labor.

ILLNESS HISTORY AND PHYSICAL GROWTH

I. CORRELATION IN JUNIOR PRIMARY CHILDREN FOLLOWED FROM FALL TO SPRING

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Textbooks in such fields as pediatrics [1] and child psychology [2] often include unqualified statements expressing the view that disease retards growth. Actually, there appears to be a paucity of published investigations relating to the problem, and existing materials are neither sufficiently comprehensive nor sufficiently conclusive to warrant such a broad generalization.

Representative studies on the relationship between physical growth and illness are those by Bowditch,[3] Woodbury,[4] Turner and others,[5] Palmer,[6] Hardy [7] and Jeans and Stearns.[8] Seven infants under 1 year of age were studied by Jeans and Stearns, a 2 year old child by Bowditch, a large sample of children under 6 years by Woodbury and fairly large samples of elementary and high school pupils in the remaining three investigations. Differential observations were obtained. Bowditch found loss in weight in his subject over periods up to one month

From the Iowa Child Welfare Research Station, University of Iowa.

1. Holt, L. E., and Howland, J.: Diseases of Infancy and Childhood, ed. 11, New York, D. Appleton-Century Co., Inc., 1940, p. 11.

2. Charles, J. W.: Physical Growth in Children, in Skinner, C. E., and Harriman, L. H.: Child Psychology, New York, The Macmillan Company, 1941, p. 56.

3. Bowditch, H. P.: The Relation Between Growth and Disease, Tr. A. M. A. **32**:371-377, 1881.

4. Woodbury, R. M.: Statures and Weights of Children Under Six Years of Age, Publication 87, United States Department of Labor, Children's Bureau, 1921.

5. Turner, C. E.; Lougee, W. W.; Sarabia, K., and Fuller, R. P.: Rate of Growth as a Health Index, Research Quart. (no. 3) **6**:29-40, 1935.

6. Palmer, C. E.: The Relation of Body Build to Sickness in Elementary School Children, Am. J. Phys. Anthropol. (supp.) **21**:7-8, 1936.

7. Hardy, M. C.: Frequent Illness in Childhood, Physical Growth and Final Size, Am. J. Phys. Anthropol. **23**:241-260, 1938.

8. Jeans, P. C., and Stearns, G.: The Effect of Vitamin D on Linear Growth in Infancy: II. The Effect of Intakes Above 1800 U. S. P. Units Daily, J. Pediat. **13**:730-740, 1938.

in relation to measles, an enlargement of the cervical lymphatic glands and a severe head cold. Jeans and Stearns found a slowing or cessation of growth in stature over periods up to six weeks in relation to pneumonia, bronchitis, laryngitis and otitis media, while following these periods there was "a period of more rapid growth, which usually compensated entirely for the earlier slowing." Woodbury found children with diseased tonsils, adenoids and carious teeth to be slightly lighter in weight than children largely free from such defects, though not appreciably different from them in stature. For a large series of elementary school children, Turner and others found the 2 per cent making the smallest annual gains in weight to have been ill more than those making average gains or higher. Basing his observations on amount of illness during the school year, Palmer found "no practically significant association between height and weight and illness." Employing the number of sicknesses between birth and time of examination, Hardy obtained "no indication of a general association" with size, rate of annual growth or build.

STATEMENT OF PROBLEM

The general purpose of the present investigation was to contribute a unit of substantial information to the study of the relation between illness history and physical growth. Specifically, the problem was to consider the association between amount of illness over a six month period and selected measures of body size and form, rate of growth and physical fitness. Intensive study was made of a single age group—approximately 5 to 6 years. The records utilized were collected to comply with the standards of technical rigor necessary for valid findings in this field.

EXPERIMENTAL PROCEDURE

Subjects.—The subjects for this investigation were 90 Iowa City white children, 54 boys and 36 girls, enrolled in the junior primary group of the University of Iowa Preschool Laboratories during the school years beginning 1937 to 1940, inclusive. They were between the ages of 4 years 9 months and 5 years 10 months at the time the fall examinations were made, and six months older at the time of the spring examinations. On the whole, the subjects were drawn from the higher socioeconomic groups. Information on occupation of the father showed 76.1 per cent in professions or in important managerial positions; 12.5 per cent, merchants or in minor managerial positions; 5.7 per cent, skilled laborers, and 5.7 per cent, semiskilled laborers.

DATA

Anthropometric records are routinely obtained for each child in attendance at the University of Iowa Preschool Laboratories. Each record consists of a series of measurements representing the child's size in the fall of the year and another series representing his size six months later. Beginning with the school year 1937-1938, the anthropometric procedure followed has been exceptionally rigorous. Both fall and spring records have been based on series of measurements taken inde-

pendently by 2 anthropometrists. Unusual care has been given to the training of anthropometrists and to maintaining high standards of reliability of measurement. The records have been accumulated to yield dependable values both on body size and form and on increments of growth over six month periods.

From records meeting all these specifications, the present study has utilized values for the following measurements: weight, stature, trunk length, leg length, arm length, head breadth, shoulder width, hip width, knee width, chest girth, arm girth, forearm girth, thigh girth and leg girth. A full description of the anthropometric technic for each of these measurements has been published by Knott.[9] All subjects were measured nude and in the erect position.

Unusually accurate records of absences from school and reasons for absence are kept for each child enrolled in the Preschool Laboratories. A school nurse inspects each child in the junior primary group each day shortly after he arrives at school. Children exhibiting symptoms of illness are sent home. Should a child fail to come to school, the nurse calls his parents to determine the reason for his absence. Absences and their causes are recorded on a "Daily Attendance Record." Although these records may not be entirely free from error, they are complete, and all have been compiled by an experienced school nurse,[10] who has spared no effort to make them valid reflections of each child's illness history.

The data on illness used in this investigation were obtained from these records. The procedure was as follows:

1. The number of school days elapsing between the fall and spring measurement dates of each child was determined.

2. The number of days each child was absent for illness between these dates and the duration of each illness were tabulated.

3. For each child, the number of days of absence for illness was divided by the number of days of possible attendance. The resulting figure multiplied by 100 is referred to as "percentage of time absent for illness" or, still more briefly, as "per cent of illness." Two of the 90 subjects were absent for illness an exceptional amount of time—upward of two fifths of the school year. Their cases are treated in the section on "Individual Cases." "Per cent of illness values" for the remaining 88 subjects ranged from 0 to 36, with a mean of 12.9. Ten per cent of the subjects were absent less than 2.3 per cent of the time, and 10 per cent were absent more than 24.8 per cent of the time.

OBSERVATIONS ON BODY SIZE AND FORM

The first step in analysis of the data was that of determining the degree of relationship between amount of illness during a six month period (fall to spring) and various measurements of body size taken at the beginning of the period. Analyses of this type were intended to indicate the possibility of using measures of body size to predict absence from school because of illness. Among the specific questions listed for consideration were: Is a child who is tall at the beginning of the school year likely to be sick during the year more or less than a child

9. Knott, V. B.: Physical Measurement of Young Children: A Study of Anthropometric Reliabilities for Children Three to Six Years of Age, Studies in Child Welfare, Iowa City, University of Iowa, 1938, vol. 18, no. 3

10. Nurse Laura Chennell.

who is short? Is there a tendency for heavy children to be ill more or less than children light in weight? Does the child with a small chest circumference tend to be absent because of illness more or less than a child with a large chest circumference? With what degree of success is it possible to estimate from a measurement of arm girth taken in the fall the percentage of time a child will be absent from school during the following six months?

Six measurements were selected as representative of body size. Distributions of the fall values of these measurements gave the means and variability constants shown in table 1.[11] From correlation of the values for each of these measurements with percentages of absence due to illness during the succeeding six months (the Pearson product-moment method being used) the following coefficients were obtained: stature, 0.01; weight, — 0.08; leg length, — 0.01; chest girth, — 0.11; arm girth, 0.09, and leg girth, — 0.06.

TABLE 1.—*Means and Variability Constants at the Beginning of the Study*

Measurement	N[11]	Mean	10th Percentile	90th Percentile	Range
Stature (cm.)	86	112.6	107.1	119.6	101.7 — 125.7
Weight (lb.)	85	43.9	36.4	51.0	34.3 — 57.3
Leg length (cm.)	84	49.6	46.5	53.3	42.9 — 56.3
Chest girth (cm.)	86	54.6	51.5	58.0	49.4 — 59.8
Arm girth (cm.)	87	17.4	16.0	18.8	15.0 — 20.2
Leg girth (cm.)	87	23.3	21.4	25.2	20.5 — 27.4

It is apparent that none of these coefficients is far from zero. In other words, as analyzed in the preceding paragraph there is no appreciable positive or negative relationship between measures of body size and amount of time absent from school for illness.

The fact that no relationship was found between body size and amount of illness does not preclude the possibility of relationship between body form and time absent for illness. Consequently, several analyses were undertaken to determine the relationship between illness history and body form. The results of these analyses may be regarded as attempts to answer the question of the relationship between amount of illness and the continuum of build from stockiness to slenderness. A total of eight indexes were selected as indicators of body form, and each index was correlated with the percentage values for absence due to illness.

An index which has been repeatedly proposed as a measure of body form is that obtained by dividing the cube root of weight by stature.

11. While the total number of subjects used in all group analyses was 88, the number for any given analysis may be less, owing to the fact that not all anthropometric records contained completed series of measurements.

There were 85 children for whom it was possible to determine this index. From correlation of these indexes with the percentages of illness a Pearson product-moment coefficient of 0.01 resulted.

McCloy [12] has developed a ratio which he considers to be "a very superior index of body build." This ratio is the cube root of "normal weight" divided by stature. The estimates of "normal weight" are obtained through a "multiple regression equation from measurements of total standing height, circumference of chest (corrected for fat), bicristal width of the hips (corrected for fat), and the width of the knee at the epicondyles," [13] It was possible to compute this index for 81 subjects. Correlation of the ratios with percentage of days of absence for illness gave a Pearson product-moment coefficient of -0.26, indicating a tendency for the stocky child to be absent the least.[14] According to Lindquist,[15] with a sample of 80 subjects it is necessary for the correlation value to exceed -0.22 to be significant at the 5 per cent level of confidence and ± 0.28 to be significant at the 1 per cent level of confidence. Obviously, however, the degree of relationship is too low to be practically useful.

Another index of body form is that of chest girth divided by stature. Correlation of this index with illness history gave a coefficient $r = -0.18$ $(N = 83)$.

Since none of the foregoing ratios revealed any high degree of relationship between body form and amount of illness, an index was devised which consisted of a composite of measurements. This index was the sum of head breadth, shoulder width, hip width and knee width divided by stature (which may be regarded as sum of head and neck length, trunk length and length of legs). Correlation of this index with illness history also gave a negligibly small coefficient ($r = -0.12$, $N = 57$).

A further possibility existed in determining the degree of stockiness of the trunk. It appeared that illness history might be related to slenderness or bulkiness of the trunk. Indexes were obtained by dividing chest girth by trunk length and hip width by trunk length. On correlating these indexes with the percentage values for days of absence due to illness ($N = 51$ in each instance), Pearson product-moment coefficients were obtained of -0.14 and 0.07, respectively.

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12. McCloy, C. H.: Appraising Physical Status: The Selection of Measurements, Studies in Child Welfare, Iowa City, University of Iowa, 1936, vol. 12, no. 2, p. 30.

13. McCloy, C. H.: Appraising Physical Status: Methods and Norms, Studies in Child Welfare, Iowa City, University of Iowa, 1938, vol. 15, no. 2, p. 37.

14. This follows since the correlation tables were set up in such a manner that a negative relationship indicated that the greater the value of the index the less the percentage of absence for illness.

15. Lindquist, E. F.: Statistical Analysis in Educational Research, Boston, Houghton Mifflin Company, 1940, p. 212.

A final attempt to discover relationship between body form and illness history was based on measures of the degree of stockiness of the left extremities. The sum of arm girth and forearm girth was divided by arm length, and the sum of thigh girth and leg girth was divided by leg length. These indexes were correlated with the percentages of days of absence due to illness and coefficients obtained of 0.04 ($N = 66$) and 0.01 ($N = 83$), respectively.

It may be concluded that no positive or negative relationship of sufficient magnitude to be useful for predictive purposes has been found between amount of illness and size or form of the body.

OBSERVATIONS ON RATE OF GROWTH

A further type of analysis was that of determining the degree of relationship between percentage values for amount of illness between

TABLE 2.—*Increment for Six Month Period*

Dimension	N	Mean	10th Percentile	90th Percentile	Range
Stature (cm.)	87	3.3	2.5	4.1	1.7 — 4.9
Weight (lb.)	83	3.0	1.2	5.2	0.0 — 7.1
Chest girth (cm.)	86	1.0	—0.2	2.1	—1.0 — 3.8
Shoulder width (cm.)	86	0.8	0.4	1.2	—0.4 — 1.7
Hip width (cm.)	84	0.4	0.2	0.6	0.1 — 1.1
Arm girth (cm.)	87	0.3	—0.2	0.8	—0.7 — 2.7
Forearm girth (cm.)	87	0.3	—0.1	0.7	—0.5 — 1.3
Thigh girth (cm.)	85	1.0	—0.2	2.2	—1.4 — 3.7
Leg girth (cm.)	86	0.6	0.0	1.3	—0.8 — 1.6

fall and spring and increments of growth for selected body dimensions. Here the series of values to be correlated each represent the same time interval. Questions listed for consideration were: Do the junior primary children who make high gains in height from fall to spring tend rarely to be absent for illness? Are the junior primary children who make little or no gain in weight during the six months from fall to spring frequently absent for illness? For the group of more than 80 young children available for study, is there any relationship between growth increments in chest circumference, hip width or arm girth and the percentage values for days absent from school for illness?

The measurements selected were stature, weight, chest girth, shoulder width, hip width, arm girth, forearm girth, thigh girth and leg girth. These particular measurements were chosen since it was thought that they were indicative of the growth of the body in its general dimensions and major segments. The increment values for each measurement were reduced to the series of figures for central tendency and variability shown in table 2.

From zero order correlation of increment values with percentages for illness, the coefficients (Pearson product-moment) were: —0.02 for stature, 0.05 for weight, 0.05 for chest girth, —0.04 for shoulder width, 0.17 for hip width, 0.04 for arm girth, —0.04 for forearm girth, —0.05 for thigh girth and —0.03 for leg girth.

A high negative coefficient for gain in weight with percentage of days absent for illness would have implied that the greater the amount of illness the lower the rate of gain in weight. It is evident, however, that neither this relationship nor its converse is found. None of the above coefficients differs appreciably from zero. In other words, as analyzed here, there appears to be no relationship between percentage of days absent for illness and semiannual increments in body dimensions.

The fact that these correlation coefficients showed no relationship between amount of increase in body size and illness history suggested that an attempt be made to discover an alternative method of treating the data which might be better suited to revealing any existing relationship. It was thought that possibly extremely slight illnesses (e. g. minor colds) have no effect on the child's growth and their inclusion in the illness figures might be obscuring the effect of illnesses of longer duration. On this hypothesis, tabulation was made of the duration of each illness which each child had during the six months. This tabulation showed a preponderance of illnesses of one or two days' duration. Specifically, it was found that 53 per cent of the illnesses required the child to be absent for only one or two days. Percentages of days of absence were recalculated to include only those illnesses which kept a child out of school for more than two days at a time. These percentages of absence ranged from 0 to 34 and gave a mean of 10.4. Ten per cent each were below 1 and above 22.2.

When percentages of absence for illnesses of more than two days' duration were correlated with stature and weight increments, the following values accrued:

Absolute Increment	N	Coefficient of Correlation with Illnesses of More Than 2 Days' Duration
Stature	87	—0.02
Weight	83	0.01

The result of this analysis fails to yield any evidence of relationship. If anything, the correlation coefficients are closer to zero than those for total amount of illness.

On the hypothesis that a particular height or weight increment is more significant if made by an initially small child than by an initially large child, it was decided to make analyses for relative (percentage) gains in stature and weight. These expressions of gain over six months in relation to size at the beginning of the period were obtained by dividing 100 times each child's gain in a particular dimension by the

absolute magnitude of the dimension at the fall examination. When the percentage gains were correlated with the percentage of days of absence for illness, it was found:

Percentage Increment	N	Coefficient of Correlation with Total Illness
Stature	87	—0.02
Weight	83	0.07

These coefficients do not support the view that there is a relationship between amount of illness and rate of growth in body size.

Percentage gains in height and weight were also correlated with percentage of days of absence for illness when the absences exceeded two days in duration.

Percentage Increment	N	Coefficient of Correlation with Illnesses of More Than 2 Days' Duration
Stature	87	.01
Weight	83	.01

Obviously, no significant difference in correlation coefficients is obtained when the absences of one and two days' duration were eliminated from the total amount of illness. The coefficients consistently fail to yield any indication of association between amount of illness and rate of physical growth.

INDEXES OF PHYSICAL FITNESS

Numerous anthropometric devices have been proposed for evaluating what different writers have called the health status, nutritional state or physical fitness of the child. These devices have been used in attempting to appraise the subject as "satisfactory" or "not satisfactory," as of "normal weight" or "underweight" or as "physically fit" or "below par."

The proposals made have been based both on the status of the individual—body size or form at a particular age—and on individual progress—increments of growth over short periods of time. As an example of appraisal of status in terms of size, the reader is referred to Oeder's [16] paper on the use of measurements of thickness of subcutaneous tissue for estimating state of nutrition. Devices for evaluating status in terms of stature and weight include the Tuxford index of nutrition [17] and tables constructed by Baldwin and Wood,[18] Peatman and Higgons,[19]

16. Oeder, G.: Die Fettpolsterdicke als Index des Ernährungszustandes bei Erwachsenen, Med. Klin. **6**:657-662, 1910.

17. Tuxford, A. W.: A Nutritional Index for School Children, Pub. Health, London **27**:377-378, 1914.

18. Baldwin, B. T., and Wood, T. D., cited by Baldwin, B. T.: Weight-Height-Age Standards in Metric Units for American-Born Children, Am. J. Phys. Anthropol. **8**:1-10, 1925.

19. Peatman, J. G., and Higgons, R. A.: Growth Norms from Birth to the Age of Five Years: A Study of Children Reared with Optimal Pediatric and Home Care, Am. J. Dis. Child. **55**:1233-1247 (June) 1938.

Manuel, [20] Steggerda and Densen,[21] Diehl,[22] and others. Systems for anthropometric appraisal of status based on individual differences in body form have been developed by Pryor and Stolz,[23] McCloy [24] and the American Health Association.[25] The use of increments of growth as a method of evaluating health has been advocated through *The Journal of the American Medical Association,*[26] by Shuttleworth [27] and by Turner and Nordstrom.[28] In the first article, the position is taken that "growth in terms of individual progress" is a better "index of nutritional health" than are age-height-weight tables. Shuttleworth has listed several points in support of the same position. Turner and Nordstrom have advocated monthly weighing of children and appraisement in terms of regularity versus intermittency of gain.

Few of the proposals for which standards have been developed have treated the age period covered in this study. Some have confined attention to the first year of life, while most others have dealt with the school ages or adulthood. There are two proposals, however, that lend themselves to consideration in the present investigation. One of these is an evaluation in terms of status—the McCloy norms—and the other in terms of progress—"poor gainers."

In the McCloy approach estimated or "expected" weight is computed from "a normal regression equation" which takes into account stature, chest girth, hip width and knee width. Estimated weight is termed "normal weight." The ratio of actual (observed) weight to normal weight is the ultimate index for apprasial of the individual. McCloy considers that children with ratios more than 6 per cent under the average "are underweight" (below par, unsatisfactory), and "may be in need of medical attention" (McCloy,[13] p. 110).

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20. Manuel, H. T.: Physical Measurements of Mexican Children in American Schools, Child Development **5**:237-252, 1934.

21. Steggerda, M., and Densen, P.: Height, Weight and Age Tables for Homogeneous Groups with Particular Reference to Navaho Indians and Dutch Whites, Child Development **7**:115-120, 1936.

22. Diehl, H. S.: Height and Weights of American College Men, Human Biol. **5**:445-479, 1933; The Heights and Weights of American College Women, ibid. **5**:600-623, 1933.

23. Pryor, H. B., and Stolz, H. R.: Determining Appropriate Weight for Body Build, J. Pediat. **3**:608-622, 1933.

24. McCloy (footnotes 12 and 13).

25. American Child Health Association: Nutritional Status Indices, New York, the Association, 1935.

26. Height-Weight-Age Tables for Children, editorial, J. A. M. A. **101**:369-370 (July 29) 1933; reprinted, Am. J. Phys. Anthropol. **18**:155-157, 1933.

27. Shuttleworth, F. K.: Standards of Development in Terms of Increments, Child Development **5**:89-91, 1934.

28. Turner, C. E., and Nordstrom, A.: Extent and Seasonal Variations of Intermittency in Growth, Am. J. Pub. Health **28**:499-505, 1938.

The data of the present investigation were analyzed using McCloy's ratio. Six children were found to be more than 6 per cent underweight at the time of the fall examination, and 4 children more than 6 per cent underweight at the time of the spring examination. Two of these children were "underweight" both in the fall and in the spring. Table 3 presents material derived from the illness histories for the following groups: (*a*) children underweight in the fall, (*b*) children underweight in the spring, (*c*) children underweight in the fall but not in the spring, (*d*) children underweight in the spring but not in the fall and (*e*) children underweight both in the fall and in the spring. The first row of figures in the table gives central tendency and variability values for the entire group of junior primary children included in the study.

On the basis of this tabulation the following statements can be made: Children underweight in the fall were absent from school during the

TABLE 3.—*Amount of Illness for Underweight Children Compared with That for the Total Junior Primary Group*

	Number	Total per Cent Absence			Per Cent Absence over 2 Days at a Time		
		25th Percentile	Mean	75th Percentile	25th Percentile	Mean	75th Percentile
Total group	88	6.0	12.9	18.8	4.0	10.4	16.5
Underweight:							
Fall	6	...	10.1	....	...	7.0	....
Spring	4	...	6.2	....	...	3.9	....
Fall but not spring	4	...	12.9	....	...	9.0	....
Spring but not fall	2	...	7.8	....	...	4.8	....
Both fall and spring	2	...	4.7	....	...	2.9	....

succeeding six months less than the average for the junior primary group. Children rated unsatisfactory in the spring were absent less during the previous six months than the average for the total group. Children under par in the fall but attaining "normal weight" by spring were absent an amount approximately equal to the group average. Children normal in weight in the fall but dropping into the "underweight" classification by spring were ill less than the average for the total group. Children underweight in the fall and remaining underweight over the six month period were in the lower or "best" quarter of the group in respect to amount of illness.

Since the illness histories of the underweight children do not show them to be absent from school more than the average amount of time for the total group, it is pertinent to note that establishment of the validity of the McCloy designation "underweight" must primarily be sought in factors other than disease (e. g., diet, exercise and rest).

A second type of appraisal that may be applied to the data used in this investigation is that utilizing increments of growth. Children were

selected who showed lowest gains over the six month period in stature, weight, chest girth, arm girth or leg girth. Table 4 presents an analysis of the illness histories for these children. From this comparison of the illness histories of children showing the smallest increments of growth (22 different children are represented) with those for the entire junior primary group, the following statements can be made: Children registering the lowest gains in stature, weight or chest girth over the six months were absent from school for illness slightly

TABLE 4.—*Amount of Illness for Children Making Lowest Gains Compared with Those for the Total Junior Primary Group*

		Total per Cent Absence			Per Cent Absence over 2 Days at a Time		
	Number	25th Percentile	Mean	75th Percentile	25th Percentile	Mean	75th Percentile
Total group	88	6.0	12.9	18.8	4.0	10.4	16.5
Children showing:							
Stature gain under 2.5 cm.	5	...	17.6	....	...	15.8	....
Weight gain under 1.2 lb.	8	...	14.6	....	...	12.1	....
Chest girth gain under 0 cm.	7	...	15.8	....	...	13.5	....
Arm girth gain under −0.3 cm.	8	...	11.1	....	...	7.7	....
Leg girth gain under 0 cm.	5	...	13.2	....	...	10.1	....

TABLE 5.—*Illness Histories of Children Showing Gains in Two or More Measurements Compared with Those for the Total Group*

		Total per Cent Absence			Per Cent Absence over 2 Days at a Time		
	Number	10th Percentile	Mean	90th Percentile	10th Percentile	Mean	90th Percentile
Total group	88	2.3	12.9	24.8	1.0	10.4	22.2
Children low in:							
Four measurements	1	...	28.4	....	...	23.9	....
Three measurements	2	...	6.8	....	...	4.7	....
Two measurements	4	...	17.9	....	...	15.1	....

more than the average of the total group. Children gaining least in arm girth were absent less than the average amount of time. Children with the smallest increments of growth in leg girth were absent an amount approximately equal to group average. None of the illness averages for the children making the lowest gains in the five dimensions fall in the upper quarter of the illness distributions for the total group.

As already mentioned, 22 children were included in the subgroups making the lowest gains in each of the five measurements: stature, weight, chest girth, arm girth and leg girth. Seven of these children showed low gains in more than one of the five dimensions. Table 5 gives illness means for the children showing low gains in four, three

or two of the five dimensions. These averages are compared with means and variability constants for the entire junior primary group.

As shown in table 5, there was 1 child registering unusually low gains in four of the dimensions studied (stature, weight, arm girth and leg girth). This child (a girl) was in the upper quarter of the total group in amount of absence for illness. According to the McCloy norms, she was of "normal weight" both in the fall and in the spring. There were 2 children who made low gains in three measurements. These children had illness history averages moderately below those for the total group. The 4 children who made low gains in two of the measurements had illness averages somewhat above the average for the entire group. None of these 6 children were "underweight" according to the McCloy norms.

INDIVIDUAL CASES

Individual study was made of the records for the 2 children not included among the 88 subjects used in the group analyses. These

TABLE 6.—*Increments over Six Month Period*

Increment	Case 919 Female	Case 6656 Male	Total Junior Primary Group		
			10th Percentile	25th Percentile	Mean
Stature	2.8	3.5	2.5	3.0	3.3
Weight	2.5	2.3	1.2	1.9	3.0
Chest girth	2.5	0.1	0.0	0.5	0.9
Arm girth	0.1	—0.7	—0.3	0.0	0.3
Leg girth	0.5	0.2	0.0	0.2	0.6

children were noted in the section on "Data" as having had exceptional amounts of illness. The percentage of time absent for illness was 42.9 for one of these children, a girl, and 67.0 for the other, a boy. For absences of more than two days' duration, the illness percentages were 40.5 and 61.6, respectively. Table 6 compares the increments of growth made by each of these children with the distributions of gains for the total junior primary group studied.

For the girl, comparison of the growth increments with the distribution of increments for the group reveals that none of her gains would have fallen in the lower tenth of the distribution for the group. Gain in stature would have fallen in the lower quarter of the stature distribution; gains in weight, arm girth and leg girth, below the respective means for these distributions, and gain in chest girth, in the upper quarter of this distribution. For the boy, loss in arm girth would have placed him with the lower tenth of the group, gain in chest girth with the lower quarter, gains in leg girth and weight at or near the twenty-fifth percentile and gain in stature slightly above the average. According to the McCloy norms, the 2 children were each of "normal weight" both in the fall and in the spring.

On the whole, the rates of growth for these 2 children are slightly below the averages for the group. However, in only 1 instance—arm girth for the boy—is the difference between fall and spring measurement sufficiently low to place it below the tenth percentile.

SUMMARY AND CONCLUSIONS

The present investigation was intended to contribute to the problem of the relationship between amount of illness and physical growth. Ninety children enrolled in the junior primary group of the University of Iowa Preschool Laboratories during the school years 1937 to 1940, inclusive, were studied over a six month period—fall to spring. Illness histories were obtained from records taken daily by a school nurse. The anthropometric records for each child were compiled from sets of independent observations made by two anthropometrists. Fourteen body measurements were utilized in the analyses.

Relationships between per cent of absence for illness during the six month period and selected measures of size and form, rate of growth and indexes of physical fitness were secured. Pearson product-moment correlation coefficients revealed no positive or negative relationship of sufficient magnitude to be useful for predictive purposes between amount of illness and size, form or rate of growth. Analysis of amount of illness for children "underweight" according to the McCloy norms gave no indication of association and suggested that factors other than disease must be sought as primarily accounting for these "underweight" appraisals. Analyses carried out for children showing low gains in stature, weight, chest girth, arm girth or leg girth and those showing low gains in two or more of these five measurements gave no clear support to the position that children manifesting exceptionally low rates of growth are absent for illness more than the average amount of time for the total sample. Children with exceptionally high percentages of absence showed, on the whole, rates of growth just slightly below the averages for the total group.

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ACUTE ANTERIOR POLIOMYELITIS IN KERN COUNTY, CALIFORNIA

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Acute anterior poliomyelitis has been reported for some time from Kern County, Calif., where the disease has been of particular importance since 1934 and 1935. During these two years the incidence increased and localized outbreaks occurred, as shown by Gifford and Bogen [1] in the annual report of the Kern County health department. Most of the cases in which there was some disturbance of the central nervous system were reported as instances of poliomyelitis from this period until late in 1938, when it became evident that, while some of the milder, nonparalytic conditions were due to the virus of this disease, many could be attributed either to the western equine encephalomyelitis virus or to the St. Louis encephalitis virus or to both, as was shown by Howitt [2] and by Buss and Howitt.[3] After laboratory differentiation was established, it was apparent that more than one variety of neurotropic virus disease was endemic in this district. All were found in the same geographic environments and had a similar seasonal occurrence, depending on the length of the warm weather. While poliomyelitis tended to be more prevalent in the urban than in the strictly rural areas, it was often found outside the city limits in suburban or farming localities away from the more crowded habitations. The inhabitants

This study was aided by a grant from the National Foundation for Infantile Paralysis, Inc.

From the George Williams Hooper Foundation, University of California Medical Center, San Francisco, and the Kern County Health Department.

1. Gifford, M. A., and Bogen, E.: Immunization Against Infantile Paralysis, Ann. Rep. Kern County Health Dept. **36**:42-80, 1935-1936.

2. Howitt, B. F.: Viruses of Equine and St. Louis Encephalitis in Relationship to Human Infection in California, 1937-1938, Am. J. Pub. Health **29**: 1083-1097, 1939.

3. Buss, W. C., and Howitt, B. F.: Human Equine Encephalomyelitis in Kern County, California, 1938, 1939 and 1940, Am. J. Pub. Health **31**:935-944, 1941.

of the city of Bakersfield had the advantage of sanitary plumbing and a city sewer system, but persons who lived in newly opened districts in close proximity to the city often depended on the backyard privy.

Since the early work of Kling, Wernstedt and Pettersson [4] and the later studies by Paul and Trask,[5] Kramer, Gilliam and Molner,[6] McClure and Langmuir [7] and others have shown that the virus of poliomyelitis can be readily recovered from human excreta; and since the further reports by Paul, Trask and others,[8] by Sabin and Ward [9] and by Toomey, Takacs and Tischer [10] attest the possibility of the fly as a carrier of this disease, it seems opportune to record the results of the limited investigations undertaken in Kern County in respect to sporadic cases of poliomyelitis in endemic areas during the past few years. The information obtained from a different locality may be added to what has been found elsewhere and help to form another link in a chain of evidence that can be evaluated later in a more comprehensive manner. Top and Vaughan [11] have suggested that studies of every phase of epidemiologic evidence in poliomyelitis, particularly in regard to the environment, are of value for this future knowledge.

METHODS

Fecal specimens were collected and kept frozen at a low temperature until shipped in dry ice to the laboratory at the Hooper Foundation in San Francisco. If not used immediately, they were stored in dry ice until needed. The stools were then treated by the ether method of Paul and Trask.[5] After twenty-four hours in the refrigerator, the ether was removed by suction and the fecal material

4. Kling, C.; Wernstedt, W., and Pettersson, A.: Recherches sur la mode de propagation de la paralysie infantile (maladie de Heine Medin). Troisième mémoire, Ztschr. f. Immunitätsforsch. u. exper. Therap. **12**:303-354, 1912.

5. Paul, J. R., and Trask, J. D.: The Virus of Poliomyelitis in Stools and Sewage, J. A. M. A. **116**:493-497 (Feb. 8) 1941.

6. Kramer, S. D.; Gilliam, A. G., and Molner, J. G.: Recovery of the Virus of Poliomyelitis from the Stools of Healthy Contacts in an Institutional Outbreak, Pub. Health Rep. **54**:1914-1922, 1939.

7. McClure, G. F., and Langmuir, A. D.: Search for Carriers in an Outbreak of Acute Anterior Poliomyelitis in a Rural Community: The Incidence of Virus in Feces, Am. J. Hyg. **35**:285-291, 1942.

8. Paul, J. R.; Trask, J. D.; Bishop, M. B.; Melnick, J. L., and Casey, A. E.: The Detection of Poliomyelitis Virus in Flies, Science **94**:395-396, 1941.

9. Sabin, A. B., and Ward, R.: Flies as Carriers of Poliomyelitis Virus in Urban Epidemics, Science **94**:590-591, 1941; Insects and Epidemiology of Poliomyelitis, ibid. **95**:300-301, 1942.

10. Toomey, J.; Takacs, W. S., and Tischer, L. A.: Poliomyelitis from Flies, Proc. Soc. Exper. Biol. & Med. **48**:637-639, 1941.

11. Top, F. H., and Vaughan, H. F.: Epidemiology of Poliomyelitis in Detroit in 1939, Am. J. Pub. Health **31**:777-790, 1941.

inoculated into monkeys of either the rhesus or the philippinensis varieties. Usually 5 cc. was given intranasally and 20 cc. intraperitoneally to the larger animals. The amounts were reduced for the smaller ones. Daily records of temperature were taken, and the monkeys were observed for evidence of fever, nervousness, irritability, tremors, muscular weakness and subsequent paralysis. If typical advanced symptoms developed, the animals were killed and the cord kept for further passage and histologic examination. Monkeys that showed doubtful symptoms were tested intracerebrally for immunity with a known poliomyelitis virus.

The flies that were obtained were ground in either saline solution or water, and after centrifugation the supernatant fluid was inoculated intranasally and intraperitoneally into monkeys. Samples of sewage were collected early in the morning near the county hospital and also from the main outlet of the city sewer. Fifteen per cent ether was added.

POLIOMYELITIS IN KERN COUNTY FOR THE PAST FEW YEARS

Twenty-seven cases of poliomyelitis were reported from Kern County in 1938, 73 in 1939, 18 in 1940 and 14 in 1941. The diagnosis was based on the clinical symptoms and usually on the absence of antibodies for either the virus of St. Louis encephalitis or that of western equine encephalomyelitis. A few persons, however, showed typical flaccid paralysis and yet their serums neutralized against the encephalitic viruses. Were the antibodies from an earlier infection, or were the three viruses present simultaneously?

Although the number of cases fluctuates each year, the general geographic distribution remains about the same, as seen in maps 1 to 4. The highest rate for poliomyelitis has occurred in the city of Bakersfield itself or just outside the city limits. The small towns of Taft and Shafter have contributed patients each year, while certain strictly rural areas have likewise been continually affected. The disease has usually reached a peak in the summer months of July and August, although in 1941 sporadic cases were reported during the seven months from April through November, with none in May and 1 to 3 in each of the other months.

One hundred and thirty-two cases of poliomyelitis were recorded during the four years 1938 to 1941, with the highest incidence, of 73, in 1939 and the lowest, of 14, in 1941. During this period more males than females were affected, although the sex distribution was reversed in the last year. The more general prevalence of poliomyelitis among the male population corresponded to the condition noticed for the encephalitides and might conform with the idea of exposure to an insect vector. When the younger children alone are concerned, however, the chances of exposure are about equal for the sexes, as noticed by Howitt [12] for encephalitis in California. For this whole period there

12. Howitt, B. F.: Human Equine Encephalomyelitis and St. Louis Encephalitis in California, 1939-1941, Am. J. Pub. Health **32**:503-515, 1942.

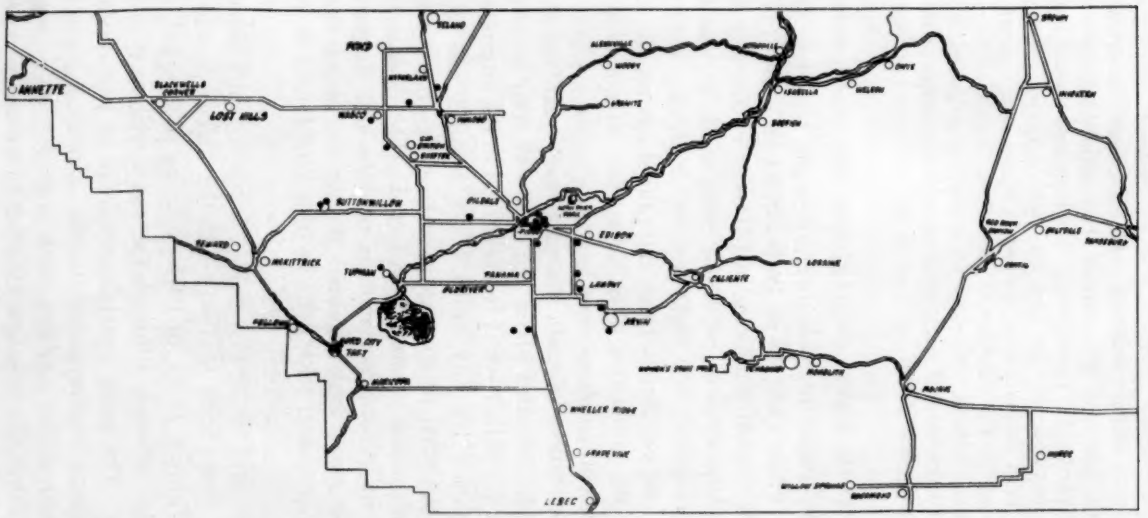

Fig. 1.—Map of Kern County, Calif., showing the main roads and towns and the geographic distribution of poliomyelitis during the year 1938.

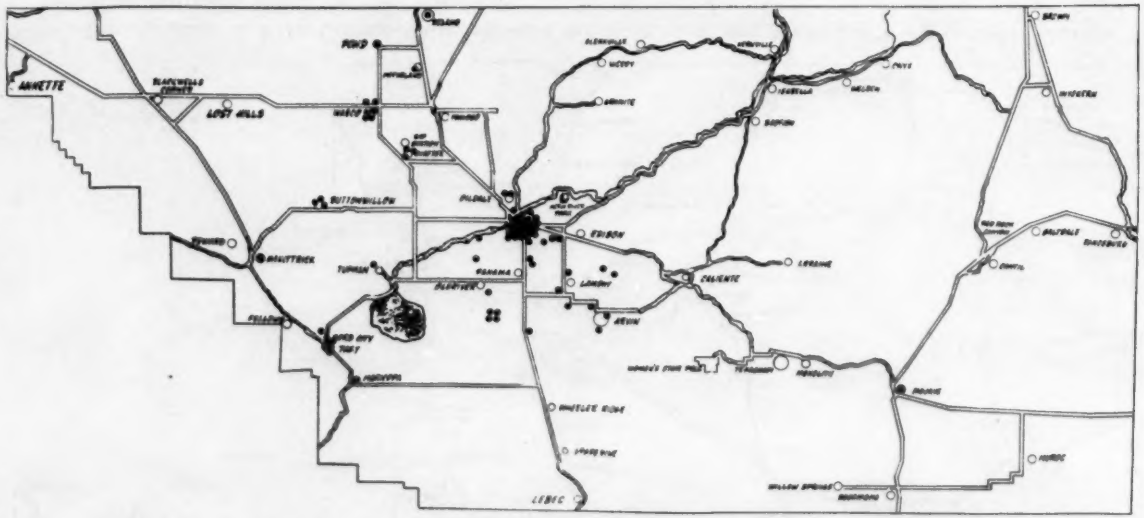

Fig. 2.—Map of Kern County, Calif., showing the main roads and towns and the geographic distribution of poliomyelitis during the year 1939.

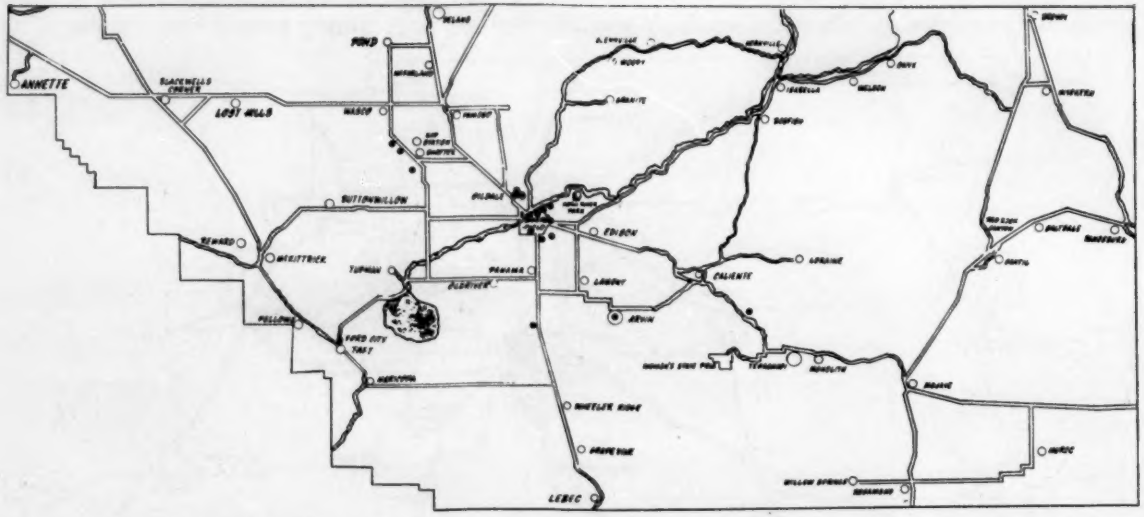

Fig. 3.—Map of Kern County, Calif., showing the main roads and towns and the geographic distribution of poliomyelitis during the year 1940.

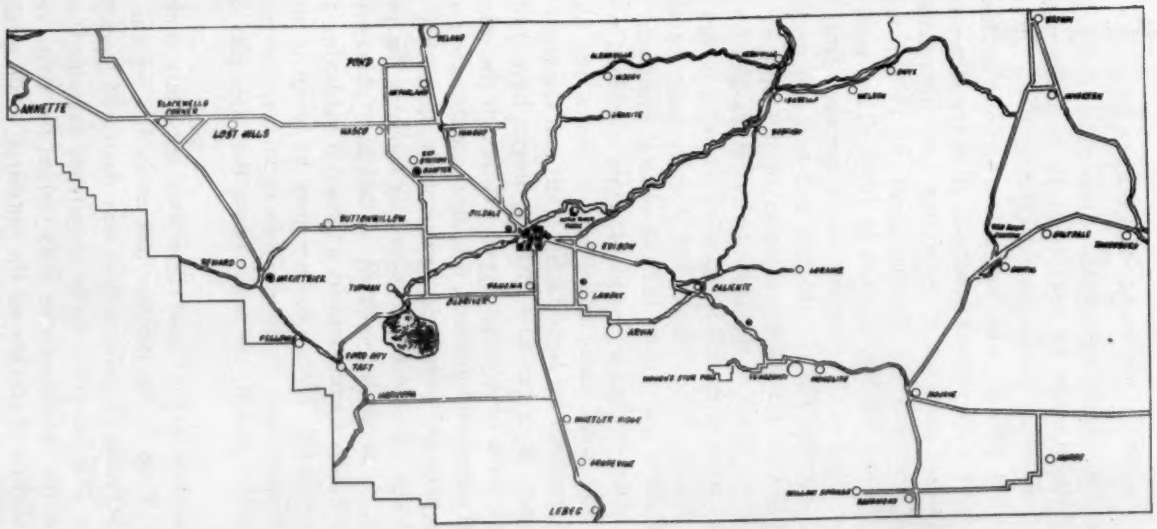

Fig. 4.—Map of Kern County, Calif., showing the main roads and towns and the geographic distribution of poliomyelitis during the year 1941.

were 63 patients with poliomyelitis between the ages of birth and 9 years, 32 between 10 and 19, 20 between 20 and 29 and 17 over 30 years of age.

RESULTS OF FECAL EXAMINATIONS

Stools from Poliomyelitic Patients.—Specimens of the stool were collected during the summer of 1941 from 19 available patients who had recovered from poliomyelitis since 1939 and 1940. Material was obtained from those persons who had shown definite evidence of the disease. Although 5 were without paralysis, all of the others had shown some type of residual paralysis, 8 recovering later after treatment.

Poliomyelitis virus was not obtained from the 11 persons with an onset in 1939 nor from the 8 with onset in 1940. They were evidently not shedding the virus at the time the single specimen from each was obtained. Eight months was the shortest and two and one-half years was the longest period preceding collection of the samples after the onset of the disease. Two of the patients had antibodies for both the St. Louis and the western equine encephalitic virus; 2 others had antibodies only for the St. Louis strain and 2 more only for the equine strain. All 6 of these had shown definite clinical symptoms of poliomyelitis. One, however, had a flaccid paralysis combined with irritability, delirium and some encephalitic signs. Since his blood gave strongly positive reactions for both the St. Louis and the western equine encephalitis viruses, it is probable that he might have had a combined attack of all three neurotropic types. Although the others might likewise have had combined infections, it is also true that their antibodies might have been acquired previously, particularly since they were all over 10 years of age. However, it is well to consider the probability that the patients occasionally reported as having "polioencephalitis" might easily have a mixed simultaneous infection if antibodies are found for the different viruses. More credence may be given to this possibility now that transmission by mosquitoes is known for two of the types of encephalitis [18] and it has been shown that flies play a role in poliomyelitis.

The season was late in 1941, and there were not many clinical cases of poliomyelitis. None of the patients had antibodies for the encephalitis viruses. The virus of poliomyelitis was recovered from the stool specimens of 4, or 28.5 per cent, of the 14 persons examined, as shown in table 1. One of the patients whose stool yielded the virus, resided in the city of Bakersfield and another on the outskirts, while a third came from the town of Shafter and a fourth lived in a rural settlement on the highway. Four of the other 10 patients for whom a diagnosis of

13. Hammon, W. McD.; Reeves, W. C.; Brookman, B.; Izumi, E. M., and Gjullin, C. M.: Isolation of the Viruses of Western Equine and St. Louis Encephalitis from Culex Tarsalis Mosquitoes, Science **94**:328-330, 1941.

TABLE 1.—*Results of Examination of Stools of Patients Suspected of Having Poliomyelitis in 1941* *

Patient No.	Initials	Age	Address	Date of Onset	Time of Collection of Stool After Onset	Neutralization Test *		Inoculation of Stool Material into Monkey	Monkey Passage †	Symptoms of Patient
						St. Louis Virus	W. Equine Virus			
1	R. J.	19	On ranch near Lamont road	April 1941	3 mo.	0	0	No virus ‡	.....	Paralysis
2	C. B.	11	City of Bakersfield	6/ 8/41	7 days	0	0	No virus ‡	.....	Muscle weakness; recovered
3	B. B.	6	City of Bakersfield	6/20/41	19 days	0	0	No virus ‡	.....	Slight residual paralysis; cleared
4	N. S.	8	Shafter	7/28/41	5 days	0	0	Virus found ‡	+ Passage	Partial paralysis of right leg; weakness in left leg
					15 days	..	..	Virus found ‡	.....	.....
					24 days	..	..	Virus found ‡	.....	.....
					39 days	..	..	No virus ‡	.....	.....
					73 days	..	..	No virus ‡	.....	.....
5	Z. G.	12	City of Bakersfield	8/ 6/41	12 days	0	0	Virus found ‡	+ Passage	No paralysis
6	A. L.	2½	Fruitvale (rural)	8/ 7/41	5 days	0	0	Monkey with symptoms ‡	Monkey immune	Weakness of both legs
7	P. P.	8	Rural	8/20/41	5 days	..	..	Virus found §	+ Passage	Residual weakness of leg; cleared
			Bakersfield		14 days	..	..	Virus found ‡	.....	.....
					50 days	..	..	Virus found ‡	+ Passage	.....
8	M. D.	6	City of Bakersfield	9/15/41	4 days	0	0	No virus §	.....	No paralysis; recovered
					20 days	..	..	No virus ‡	.....	.....
9	M. W.	29	Rural Bakersfield	10/ 1/41	8 days	0	0	No virus §	.....	No paralysis
					15 days	..	..	Monkey weak and died §	To M2850 No virus	.....
10	J. H.	23	Keene (rural)	9/11/41	35 days	0	0	No virus §	.....	No paralysis
11	C. B.	22	City of Bakersfield	10/26/41	3 days	0	0	Left arm and leg weak; died §	To M2856 No virus	No paralysis
					20 days	..	..	No virus §	.....	.....
12	M. F.	13	City of Bakersfield	10/16/41	3 days	0	0	No virus §	.....	No paralysis
13	E. B.	5	City of Bakersfield	11/28/41	7 days	0	0	No virus §	.....	No paralysis
14	H. D.	6	McKittrick (rural)	11/14/41	21 days	0	0	No virus §	.....	Weakness of some muscles; recovered

* 0 indicates that serum did not neutralize the virus.
† + indicates typical poliomyelitis.
‡ Inoculated into a rhesus monkey (Macaca mulatta).
§ Inoculated into a Philippinensis monkey.

poliomyelitis was made but from whom the virus was not recovered resided in the city of Bakersfield, where sanitary plumbing was available, while the other 6 came from rural communities either immediately outside of Bakersfield or at some distance from the larger towns on small farms where privies were installed.

A specimen from patient 1 was not obtained until three months after the onset. One of the other first three samples that failed to contain the virus was likewise collected several weeks after the acute symptoms of the disease. All 4 patients from whose stools the virus was obtained contracted poliomyelitis late in July or in August, during the warmest weather.

Specimens from patient 4 obtained five, fifteen and twenty-four days after the onset contained the poliomyelitic virus, but not those collected in thirty-nine and seventy-three days. Three specimens containing the virus were received from patient 7, extending over a longer period, five, fourteen and fifty days from the onset. Only one virus-containing specimen was obtained from each of the patients 5 and 6, received twelve and five days respectively after the first symptoms.

It was likewise of interest to find that ground fecal material with the ether removed could be kept for some time in the dry ice refrigerator at — 70 C. and still retain virulence. Specimens from patient 4 and from one of his contacts were left frozen for nearly four months, when they were found capable of infecting monkeys, although the incubation period was prolonged twelve to twenty-two days. Likewise unground specimens can be left for varying periods of time at the low temperature and still contain viable virus. For nine virus-containing specimens the interval between the date of collection and the period of inoculation varied from seven days to five and one-half weeks, with an average of sixteen and seven-tenths days.

Stools from Contacts.—Fecal material was also collected from 31 of the close contacts of the patients whose stools had been found to contain the virus (table 2), more than one sample being obtained from some of them. Seven (18.4 per cent) of the 38 specimens tested produced evidence of the virus in monkeys. Two of these samples came from 1 person.

The animal given the material from contact 1 showed a mild and atypical course but was immune on subsequent intracerebral inoculation of known virus. Contact 1 was the mother of patient 3, from whom no virus was recovered and whose symptoms were likewise atypical. Of the monkeys that were inoculated with specimens from 3 contacts of patient 4, 2 had typical poliomyelitis, but the third had a mild, atypical course and the virus could not be transferred. A second sample from one of the contacts whose stools had contained the virus, obtained

twenty-eight days later, produced mild symptoms in an animal, but the virus was not recovered on second passage.

Fecal specimens were collected from 6 children who were in close association in school with patient 8. The results were negative with 5 samples, but a sample of the stool from the sixth child produced slight paralysis in a monkey.

Table 2 indicates the age groups of the contacts whose feces were examined and the length of time elapsing between collection of the specimens and first contact with the patient. Feces containing virus were obtained both early and late, and all except a single sample came from children. If more samples had been taken, it is probable the number of virus-containing specimens from the adult group would have been greater.

TABLE 2.—*Results of Examinations of Stools of Contacts of Patients Who Had Poliomyelitis in 1941* *

Age Groups in Years	Number of Contacts	Time in Days When Stools Were Collected After Contact with Patient *							
		5	7	10-11	14	21	28	35	38
1-10	17	2	1 (1+)	5	6 (1+)	1	1	2	2
11-20	6	0	3 (1+)	2	0	1	2 (3+)	0	1
Over 20	8	2	2	2	0	0	3 (1+)	0	0
Totals	31	4	6 (2+)	9	6 (1+)	2	6 (4+)	2	3

* + indicates a specimen from a stool which contained the virus of poliomyelitis.

CASE HISTORIES OF THE PATIENTS WITH VIRUS-CONTAINING STOOLS

The following brief histories are given for the patients from whose feces the poliomyelitic virus was isolated.

CASE 4.—N. W. S., an 8 year old white boy, was admitted to the Kern County General Hospital on Aug. 1, 1941, for observation for suspected anterior poliomyelitis. On his admission fever, headache, malaise, loss of appetite, delirium and weakness of the muscles of the back were noted. The physical examination showed a temperature of 102.6 F., a rigid neck, slight tenderness of the abdominal muscles and somewhat less tenderness of the muscles of the back and lower extremities. The Mantoux tuberculin and the coccidioidin cutaneous tests gave negative results, as did culture of material from the throat for diphtheria. The hemoglobin content of the blood was 90 per cent; the color index, 1.0; the red cell count, 4,400,000; the white cell count, 11,300, and the differential count, 20 per cent lymphocytes and 80 per cent polymorphonuclear cells. The Kahn and Wassermann reactions of the blood and of the spinal fluid were negative. The spinal

fluid was clear and colorless, with a 1 plus reaction for globulin, a cell count of 196 per cubic millimeter and a differential count of 57 per cent lymphocytes and 43 per cent polymorphonuclear cells.

After twenty-one days of quarantine the patient was transferred to the children's ward for further treatment. The orthopedic examination showed that all the muscles of the left leg were weak, the tendon of the left quadriceps muscle gave a very slight reaction, with remaining function 50 per cent of normal. Orthopedic appliances were prescribed for day and night use. At the present time residual paralysis is very definite in the left leg.

The reactions of the serum neutralization tests were negative for both the western equine and the St. Louis encephalitic viruses on the fifth day after the onset, but the virus of poliomyelitis was recovered from a stool specimen collected on the same day.

The patient was discharged from the hospital on Feb. 23, 1942.

CASE 5.—Z. G., a white girl 12 years of age, was admitted to the Kern General Hospital on Aug. 8, 1941 for observation for suspected poliomyelitis.

On admission she had a high fever, headache, sore throat and slight backache. The sore throat, headache and chilly sensations had been noticed on August 6, while on the day of admission there was accompanying diarrhea.

The physical examination revealed an essentially normal state except for acute pharyngitis and some injection in the right ear. Roentgenograms of the mastoid cells taken on August 9 showed nothing abnormal. The hemoglobin content of the blood was 75 per cent; the color index, 0.9; the red cell count, 4,130,000; the white cell count, 7,200, and the differential count, 16 per cent lymphocytes and 84 per cent polymorphonuclear cells. Kahn and Wassermann reactions of the blood and of the spinal fluid were negative. Cultures of material from the nose and throat yielded neither diphtheria bacilli nor hemolytic streptococci. The Mantoux tuberculin and the coccidioidin cutaneous tests produced negative reactions. The spinal fluid was clear and colorless, with a negative reaction for globulin, 10 cells per cubic millimeter and a differential count of 50 per cent lymphocytes and 50 per cent polymorphonuclear cells.

There were no abnormal developments during the stay in the hospital except a temperature of 99 to 104 F. for the first few days. A check of the muscles on the twentieth day after onset showed them to be completely normal, while reactions of the serum neutralization tests were negative for the viruses of western equine encephalomyelitis and of St. Louis encephalitis. A stool specimen obtained on the twelfth day after the onset contained the virus of poliomyelitis.

The patient was discharged from the hospital on August 27 as having made a complete and uneventful recovery.

CASE 6.—A. S. L., a 2½ year old white boy, was admitted to the Kern General Hospital for observation for anterior poliomyelitis or possible tuberculous meningitis.

For three days prior to admission the child had shown fever, intractable crying and inability to stand or walk. On his admission to the hospital the physical examination showed extreme stiffness and rigidity of the neck and a pronounced tenderness of the muscles, particularly of the lumbar muscles. He could move his legs but refused to stand or walk. Mantoux tests and roentgenograms of the chest showed no evidence of tuberculosis. The Kahn and Wassermann reactions of the blood and of the spinal fluid were negative. The spinal fluid showed a ground glass appearance and had a 1 plus reaction for globulin. The cell count

was 424 per cubic millimeter and the differential count 90 per cent lymphocytes and 10 per cent polymorphonuclear cells. The blood had a hemoglobin content of 75 per cent, a color index of 0.9, 4,100,000 red cells, 10,600 white cells and a differential count of 32 per cent lymphocytes and 68 per cent polymorphonuclear cells. The stained smear was normal. The serum neutralization tests gave negative reactions for the western equine and the St. Louis encephalitis viruses.

A stool specimen obtained on the fifth day after onset contained the virus of poliomyelitis.

CASE 7.—P. A. P., a Spanish girl 8 years of age, was admitted to the Kern General Hospital on Aug. 21, 1941 for observation for anterior poliomyelitis or possible encephalitis.

On admission she showed soreness of the muscles of both legs, more pronounced on the right, together with general muscular weakness.

The observations at physical examination were essentially normal except for a flaccid paralysis of both legs. The ankle and knee reflexes were both absent, and the triceps reaction was impaired on both sides. There had been a history of high fever for five days and some generalized pain in the knee joints. The results of laboratory tests were completely normal, including those on the spinal fluid, which had only 8 cells, all lymphocytes, on August 21. The Mantoux tuberculin and the coccidioidin cutaneous tests, the cultures of material from the nose and throat, the Widal and undulant fever agglutination tests and the cultures of the stools for typhoid-dysentery organisms all gave negative results. Examination of the blood showed: hemoglobin, 85 per cent; color index, 0.9; red cells, 4,300,000; white cells, 26,300, and differential count, 13 per cent lymphocytes and 87 per cent polymorphonuclear cells. The stained smear was normal.

At times during the stay in the hospital the child showed definite irritability and a slight stiffness of the neck and complained of frontal headaches. In addition to the pain in the neck, the fingers of the right hand showed some swelling and painful reactions. Because of the temperature, which ranged from 99.4 to 103 F. during the first seventeen days, the low sedimentation rate, of twenty minutes, and the pains in the joints, acute rheumatic fever was suspected. However, this was definitely ruled out by the negative findings during the hospital stay and the later check-ups.

At the end of the quarantine period the acute symptoms had completely subsided, and a check of the muscles showed them to be normal. The virus of poliomyelitis was found in a stool specimen obtained on the fifth day after onset, while the serum neutralization tests for western equine encephalomyelitis and St. Louis encephalitis produced negative reactions.

The patient was discharged from the hospital on September 17 as having made a complete and uneventful recovery.

EPIDEMIOLOGIC ASPECTS

In order to stress the epidemiologic importance of these rural cases of poliomyelitis and to indicate how the virus might be disseminated in a community, the following environmental details are given for 2 of the patients (cases 4 and 7) and their contacts.

Epidemiology of Case 4.—The family (S) of patient 4 consisted of the parents, the father a gardener, and 5 children, of whom the patient was the youngest. The others ranged in age from 10 to 16 years. They were living in the small town of Shafter when the boy became ill on July 28, 1941 and was taken to the

hospital in Bakersfield. All of the children had been attending a summer play school in Shafter up to the time of the child's illness. They came home for lunch every day. The school had sanitary toilets and used the city water supply. No child in the school had been sick or had had a cold until the patient's attack of poliomyelitis developed. None became ill later. This was ascertained by personal interviews with the mothers of most of the school children.

The home of the S family was clean, well cared for and with modern plumbing facilities and city water. There were a garden, a small fish pond and a large tree nearby. The only animals on the place were several canaries in an outdoor aviary near the pond. A dog was kept next door, and chickens were on a place across the street. Water from the pond and droppings from the canaries were collected a few days after the patient became ill. Poliomyelitis virus was not obtained from these sources.

After the patient was taken to the hospital, the family moved from Shafter to another home, about ½ mile (0.8 kilometer) away in a rural district, where an open privy behind the house was in use. Six days after they arrived and one week after the onset of the symptoms of patient 4, specimens of the stools were collected from members of the family, all of whom were in good health, and material was washed out from the privy. The virus of poliomyelitis was recovered from the feces of the 2 youngest children and also from the specimen from the privy, but not from the other specimens examined. Second samples were collected from the privy and from members of the family two weeks later; the virus was isolated from the stools of 2 children, 1 of whom had had virus-containing feces on the first occasion and the other of whom had not. The virus was not obtained this time from the privy. About 198 common house flies (Musca domestica) collected from the Shafter residence and from the new home failed to give poliomyelitis to monkeys.

From the results of this investigation it seems likely that the 2 healthy contacts whose stools contained the virus were probably infected with the virus at the same time as the sick patient but failed to have clinical manifestations of the disease. They were capable of shedding the virus, however, and of contaminating the open privy where flies were found. Since the new home was in an open rural district, away from other houses and without children in the neighborhood, no other cases developed, although the possibilities for dissemination of the virus were evident if flies and fecal excreta play an active role. It was of interest that the virus of poliomyelitis could be found in the privy washings, indicating that it can withstand the products of decomposition together with the heat of summer. On the day of the first collection the temperature at Shafter was between 78 and 80 F. The mean average temperature for August 1941 for Kern County was 79.1 F., while the normal August average for the county is 82 F., as recorded by the weather bureau at the Kern County airport.

Epidemiology of Case 7.—The family of patient 7 (P) consisted of the parents and 3 children, who were the patient, an older sister and a younger brother. They lived in the outskirts of the city of Bakersfield in a clean, well kept place with a garden but with a privy in the backyard. Next door dwelt a family with 5 children. They had chickens, a dog, many flies and an open privy near the connecting fence.

The patient was taken ill on Aug. 20, 1941. Five days earlier, she had been swimming in a pool nearby and had skated violently in the evening. Her sister went with her but remained well. The neighbors' children likewise had been swimming with them. On August 23 the youngest child of the family next door became ill and was taken to the hospital but was discharged within a few days. A child who had poliomyelitis in 1939 had been living two houses north of these families but had moved the previous June.

Fecal specimens were collected from all members of both families under consideration and also from the two privies. Flies and chicken feces were likewise obtained. Virus was recovered from the stools of patient 7 but not from any of the others. The monkey given the material from the neighbors' privy, however, showed a partial paralysis of one leg and withstood an intracerebral inoculation of known poliomyelitic virus. Over five hundred house flies were collected from between the two places, but unfortunately inoculations of monkeys with them failed to produce the disease.

Once again the privy was demonstrated as a potential source of live virus. If the neighbors' child had an abortive attack of poliomyelitis, however, there was probably a common source of infection, since his illness developed three days after that of this patient. The more demonstrable attack of the latter may have been aggravated by the violent exercise before the onset.

COMMENT

The finding of the virus of poliomyelitis in human excreta and the inauguration of an attempt to isolate virus from this source as a routine procedure in laboratories equipped for this work have greatly altered former concepts as to the route of infection and the epidemiology of this disease. If the virus is excreted through the intestinal tract, there must be a way by which it enters the body. Elimination of virus in the feces, however, does not necessarily exclude the earlier theory of the nasopharyngeal portal of entry. More than one route of infection for this disease may be considered. Direct contact may explain certain outbreaks in urban and crowded communities, while in rural and isolated places one can easily understand the possibility of infection from feces, perhaps through some intermediary agent like the fly or even a biting insect.

Lumsden [14] has collected data in regard to so-called "sporadic" poliomyelitis in Tennessee during 1938 and 1940 and has been impressed by the spotty distribution of the disease with lack of any definite correlating factor. Cases were reported from unrelated places and at varying intervals, so that there was little evidence for or against either route of infection or for a "casual connection between cases or for a common source of infection." Many cases occurred in country homes

14. Lumsden, L. L.: Sporadic Poliomyelitis with Special Reference to the Geographical and Chronological Distribution in Tennessee in the Eighteen Months Ended June 30, 1940, Pub. Health Rep. **56**:992-1007, 1941.

where poor sanitation was encountered together with insects, but on the other hand cases were likewise found in urban districts. However, Lumsden mentions that there may be doubt as to the exact nature of the etiologic agent involved in each case, since no differentiation of viruses was made.

A somewhat analogous situation probably exists in Kern County, Calif., except that more differential laboratory aid has been available for the past few years. Cases of poliomyelitis have appeared continuously in the strictly urban districts as well as in the towns, usually in the same general localities each year but not necessarily in the exact neighborhood. No one carrier or source has been established, and, particularly in 1941, the cases have occurred over many months and without direct contact from one patient to the other. Prior to November 1938, the sewage from the city of Bakersfield had not been chemically treated but was filtered through leaching trenches and ran off on the ground in a southwesterly direction about 5 miles (8 kilometers) out of the city, where there were no habitations. After 1938 a modern plant for chemical treatment was installed, and little danger of spread of infection from sewage was left. In 1939, soon after the new system had been inaugurated, many cases of poliomyelitis developed around the city. However, the prevailing winds did not blow from this district toward the town; hence flies would hardly have been disseminated from this region.

Poliomyelitis virus was not recovered from the flies examined or from the nine samples of sewage obtained during 1941, when only sporadic cases were reported in Kern County. The work of others [15] has shown that both these materials are possible sources of virus especially during epidemic periods; hence negative results might be expected perhaps during this nonepidemic interval. Likewise the number of flies collected was probably insufficient for demonstration of the virus. However, the recovery of virus from specimens from privies was another proof of the hardiness and resistance of this agent to the adverse environmental factors of heat and decomposition. Such an environment might easily be a reservoir from which a vector or intermediary host could be infected, although the virus did not remain long in the places examined.

The situation in Kern County, although somewhat similar to that in Tennessee, was unlike that reported by Langmuir [16] and McClure and Langmuir [7] for a rural outbreak in the state of New York, where cases suddenly occurred in a certain district where none had been known for nineteen years. The authors were able to recover the virus

15. Kling and others.[4] Paul and Trask.[5] Kramer and others.[6] McClure and Langmuir.[7] Paul and others.[8] Sabin and Ward.[9]

16. Langmuir, A. D.: Carriers and Abortive Cases in a Rural Poliomyelitis Outbreak, Am. J. Pub. Health **32**:275-281, 1942.

from a high percentage of fecal specimens (70 to 80 per cent), not only from patients with active poliomyelitis but from both well and sick contacts. In the present study more virus-containing specimens might have been recorded if the first few patients had been examined at an earlier date. However, it may be worth emphasizing that, although separated by many miles, the patients from whom virus was obtained all became ill with poliomyelitis within three weeks of each other during midsummer, and the agent persisted for at least fifty days in the excreta of 1 child. Piszczek, Shaughnessy, Zichis and Levinson [17] have also reported on a suburban outbreak of poliomyelitis where the factor of contact was of particular significance. The virus was likewise present in the feces of healthy contacts.

From the results of this report and from what has been stressed by Top and Vaughan [11] and again recently by Sabin and Ward,[9] it would seem worth while to continue more detailed studies of both insect and animal material from these rural localities in an endeavor to ascertain more definitely the role of environmental factors in the distribution of rural poliomyelitis. Great care, however, should be taken to evaluate accurately the nature of the disease in each case and to obtain laboratory and clinical differentiation of true poliomyelitis from the summer encephalitides which so frequently appear simultaneously in the same communities.

SUMMARY

Cases of poliomyelitis occur each year in the same geographic areas of Kern County, Calif., not only around the city of Bakersfield but in certain rural districts. The height of the incidence is usually in July or August but may continue into the autumn if the warm weather persists.

There were more male than female patients during the years 1938 to 1941, and more children 9 years old and younger than persons in the older age groups.

Examination of fecal specimens collected in 1941 from 11 persons with an onset of the disease in 1939 and from 8 affected in 1940 failed to show the presence of the poliomyelitis virus.

Stools from 4 (28.5 per cent) of the 14 patients for whom a diagnosis of poliomyelitis was made in 1941, however, yielded the virus. Three of these patients lived under rural or semirural conditions, and the active agent was recovered from the privies of two families.

Poliomyelitis virus was obtained from the feces of 1 patient in five, fifteen and twenty-four days but not in thirty-nine or seventy-three days after the onset of the disease and from another in five, fourteen and fifty days after the appearance of the first symptoms.

17. Piszczek, E. A.; Shaughnessy, H. J.; Zichis, J., and Levinson, S. O.: Acute Anterior Poliomyelitis: Study of an Outbreak in West Suburban Cook County, Ill.; Preliminary Report, J. A. M. A. **117**:1962-1965 (Dec. 6) 1941.

Diluted specimens of stools kept for four months at —70 C. contained active virus, while the virus remained viable in frozen untreated feces for periods varying from seven days to five and one-half weeks before being inoculated into monkeys.

The feces of 7 (22.5 per cent) of 31 healthy contacts of patients with poliomyelitis gave evidence of the virus when inoculated into monkeys. All contacts except 1 were children.

No virus was obtained from nine samples of sewage, from bird and chicken feces or from a limited number of house flies collected during this interepidemic period.

Dr. Joseph Kent Smith, formerly of the Kern County Health Department, helped to obtain financial aid from the Kern County Committee for Infantile Paralysis. Mr. William van Herick gave technical assistance.

PEPTIC ULCER IN CHILDHOOD

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Because of the increasing frequency with which the occurrence of peptic ulcer in children is reported, the subject continues to command the greater interest of those who are called on to investigate the problem of obscure abdominal pain in children. The term obscure is used advisedly, because, as a subsequent study will show, this symptom of the disease as it occurs in children is atypical. For this reason the diagnosis of peptic ulcer in childhood is probably overlooked in many instances. The number of cases reported in the literature has now reached over 50. The cause of the disease in the child, as in the adult, remains obscure if ulceration such as is seen associated with melena in the newborn and that associated with extensive body burns, malnutrition, sepsis and similar conditions are omitted. Some authors are inclined to emphasize the greater frequency of the disease in children of the low income groups, assuming that dietary deficiency plays a role in the causation of the disease. This claim will bear scrutiny, because the studies of the disease have never been conducted on a cross section of the juvenile population but rather have been made on groups of children attending outpatient clinics of general hospitals. Among the children of the high income groups the disease will undoubtedly be found in greater frequency if it is kept in mind as one of the causes of indeterminate abdominal pain and the necessary roentgen studies are made.

The importance of focal infection in the production of peptic ulcer attracts attention by the high incidence of such ulcers associated with acute infectious disease found in the form of acute lesions in routine postmortem examinations following death from such disease. There is no doubt that the demonstrable foci of infection cannot be found in instances of peptic ulceration aside from specific ulcerations, such as those due to tuberculosis or syphilis. The generally accepted opinion is that specific bacterial infection plays little or no role in causing chronic peptic ulcer. The demonstration by pathologic study that so-called antral gastritis is invariably associated with ulcers suggests to one school of pathologists that a nonbacterial inflammatory process in the gastric mucosa is the important element in the pathogenesis of the disease. Such gastritis without ulcers in the adult can be seen in stomachs removed by subtotal gastrectomy from patients in whom the

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whole gamut of symptoms has been run, from simple postprandial pain to massive hemorrhage. The transition from gastritis to simple erosion to deep ulceration has been delineated by numerous pathologists, and the stages can be seen side by side in a single specimen. The objection to the gastritis as the etiologic factor comes especially from the gastroscopists (Schindler and others), who have repeatedly emphasized that the in vivo pictures of ulcerations usually show the mucosa about the ulcer to be normal and contend that the histologic picture seen in the specimens resected at operations is due to the interference with the blood supply to the stomach and the acid digestion during the period required for resection. Whether the theory that gastritis produces erosions which lead to ulcerations, first acute and later chronic, stands or falls, the fact still remains that the cause of the precipitating gastritis will remain entirely obscured. Trauma can undoubtedly be a direct cause of peptic ulcer, but this factor did not enter into any of the case histories which are being reported on here. That infarction with necrosis of the gastric or duodenal mucosa and ulceration is a factor in the pathogenesis of the disease is doubtful. The vascularity of the intestinal tract is extensive, and the thrombosis of vessels described at the base of ulcerative lesions is generally regarded as a result rather than a cause of the disease. The chemical theory of the causation of the disease can be summarized briefly as follows: (*a*) Peptic ulcer occurs only in those portions of the gastrointestinal tract exposed to acid gastric secretion. (*b*) Peptic ulcer will not occur in the complete absence of gastric juice. This is strikingly illustrated by the absence of peptic ulcer in adults with pernicious anemia, due to the associated achlorhydria: (*c*) Experimentally it is emphasized that chronic peptic ulcers are produced consistently by methods which prevent the neutralizing, diluting or buffering of the gastric contents as they pass from the stomach. Largely through the studies of Cushing the attention of the gastroenterologists has been turned to the diencephalon, through which the parasympathetic nervous system mediates influences which will affect the upper part of the intestinal tract. Stimulation of this center, in fact, will produce hyperemia of the gastric mucosa and will increase gastric motility, hypertonus and hypersecretion. The parasympathetic apparatus is furthermore known to be strongly influenced by cortical or psychic influence (Pavlov), and through it an approach is opened for the effect of psychogenic factors in the causation of the disease.

As regards the actual frequency of the disease, it is true that peptic ulcer in childhood is comparatively rare. In a study of records of postmortem examinations, Perry and Shaw [1] found 70 instances of the disease in 17,650 autopsies, an incidence of 0.4 per cent. Other

1. Perry, E. C., and Shaw, L. E.: Guy's Hosp. Rep. **50**:171, 1893.

similar studies have indicated that the incidence is more nearly 0.1 per cent. Bloch [2] in analyzing 450 cases of peptic ulcer found 12 patients under 20 years of age who had symptoms dating from three to five years earlier; many of the adult patients from 25 to 35 years of age had had symptoms fifteen years earlier. Hirsch,[3] in studying 10,845 cases, found the incidence between 0.3 and 1 per cent in children. Proctor [4] at the Mayo Clinic found that of 1,000 consecutive patients with gastric ulcers 16 had had symptoms from childhood and that of 1,000 consecutive patients with duodenal ulcer 26 had had symptoms from childhood. Cackovic [5] found an incidence of 2.32 per cent in children up to 10 years of age and 7.5 per cent in children up to 14 years. These figures are far in excess of those generally cited for the incidence of the disease. The sex incidence is interesting in that, unlike the striking preponderance of men among the adult victims, the distribution of the disease is regarded as equal between the sexes in childhood. This has led one group of authors (Saltzstein, Farbman and Sandweiss [6]) to postulate the theory that as puberty approaches and the estrogens are elaborated by the female these substances exert a specific effect in protecting the mature woman from the occurrence of peptic ulcer. Estrogens have been administered to adult patients for therapeutic purposes, but the results are not particularly striking. In none of the patients in the series of cases about to be described were there gross stigmas of endocrine disease.

REPORT OF CASES

CASE 1.—M. L., a 9 year old boy, was seen on Oct. 7, 1939 with a history of abdominal pain of three weeks' duration unassociated with nausea or vomiting, and bearing no distinct relation to meals. The pain did not interrupt sleep at night. A physical examination showed nothing abnormal. The child was observed for two months, during which time antispasmodics were administered but complete relief was not obtained at any time. On Feb. 2, 1940 roentgenograms of the gastrointestinal tract revealed a characteristic niche of ulcer in the proximal portion of the duodenum. The boy was given a bland diet of the Sippy type and colloidal aluminum hydroxide after meals, with complete relief of symptoms. Blood was never present in the stool. Roentgenograms taken on March 25, June 13 and September 17 showed no significant change in the crater of the ulcer. Despite this fact, the child remained free of symptoms and gained 11 pounds (5 Kg.) in weight. On Feb. 2, 1941 a fever developed, with a temperature near 101 F., associated with periumbilical pain and vomiting. The fever promptly

2. Bloch, L.; Bronstein, I. P., and Serby, A. M.: Chronic Peptic Ulcer in Children, J. A. M. A. **98**:2184 (June 18) 1932.

3. Hirsch, W.: Monatschr. f. Kinderh. **63**:249, 1935.

4. Proctor, O. S.: Surg., Gynec. & Obst. **41**:63, 1925.

5. Cackovic, cited by Crohn, B. B.: Affections of the Stomach, Philadelphia, W. B. Saunders Company, 1927.

6. Saltzstein, H. C.; Farbman, A. A., and Sandweiss, D. J.: Endocrinology **27**:400, 1940.

subsided, and the patient was discharged in three days. A roentgenogram made at that time was interpreted as showing a deformity of the duodenal bulb such as is seen in cases of healed ulcer. The boy was seen at bimonthly intervals up to about three months ago. During that time he was on a varied diet without medication and was entirely well.

CASE 2.—J. C., a 9 year old boy, was seen on Feb. 7, 1940, complaining of epigastric pain of two years' duration. The pain was knifelike, unrelated to meals and unassociated with vomiting and nausea. Physical examination disclosed nothing abnormal except a congenital cardiac murmur. Roentgen examination of the gastrointestinal tract revealed an irregularity in the contour of the lesser curvature aspect of the duodenal bulb typical of duodenal ulcer. On institution of a diet of the Sippy type with colloidal aluminum hydroxide the symptoms promptly subsided. The child gained weight, and a roentgenogram taken about six weeks later (March 15) showed no abnormality in the duodenal bulb.

CASE 3.—M. R., a boy aged 11 years, was seen Sept. 12, 1940. He had been well until December 1939, when he had an attack of stabbing substernal pain associated with nausea and vomiting, from which he recovered in one week. After that time there were many similar episodes. The child himself noted that the symptoms were relieved by meals and were worse at night. On physical examination he appeared thin and pale, and tenderness was present on deep pressure in the right upper quadrant of the abdomen. A benzidine test of the stools gave a 4 plus reaction for blood. The hemoglobin content was 80 per cent. Chemical examination of the blood revealed nothing abnormal. Three days after admission he vomited a large amount of black vomitus and passed a large tarry stool. The hemoglobin content had dropped to 58 per cent. The presumptive diagnosis of bleeding ulcer was made and a Sippy diet with alkali instituted. On the fifth day in the hospital he complained of weakness and vomited a large amount of bright red blood; the percentage of hemoglobin dropped to 32. Treatment for shock was instituted, with intravenous therapy and transfusion. The same day another profuse hematemesis occurred. Transfusion was repeated on that and the following day. The child improved gradually, and three weeks after his admission roentgenograms of the gastrointestinal tract revealed the presence of a constant deformity of the duodenal bulb characteristic of duodenal ulcer. The child was discharged on October 24 in good condition and with a hemoglobin content of 86 per cent. He remained on a bland diet with alkalis and, except for transient episodes of epigastric pain unassociated with vomiting, was well until Feb. 25, 1941, when epigastric pain became very severe and vomiting of blood-streaked material occurred and he was brought back to the hospital. Roentgenograms made soon thereafter again revealed the deformity found on the previous admission. He became free of symptoms and was discharged on March 20. Operation at that time was suggested but was refused.

CASE 4.—A. S., a 12 year old boy, was seen on Oct. 27, 1940 with a history of an attack of short duration of periumbilical pain three weeks before admission. Six days before his admission three such attacks had occurred. The mother noted that relief could be obtained if the child drank milk. There was no vomiting or melena. Roentgenograms made soon after he was admitted showed a persistent deformity of the duodenal bulb. Analysis of the gastric contents after a test meal showed normal amounts of free and total acid in the fasting contents but a high continuous rise with the meal. With routine care the symptoms rapidly disappeared, and he was discharged on November 13. Two months later he reported that there

had been some recurrence of pain, but six months later he stated that he was entirely free of symptoms.

CASE 5.—E. Z., an 8 year old boy, was seen on Jan. 26, 1941 with a history of moderate hematemesis on the day of admission. Nausea but no pain had been present for three weeks, at the beginning of which time the mother noted that the child had passed a bloody stool. Physical examination showed nothing abnormal, and no source of bleeding in the nasopharynx could be found. A roentgenogram revealed a deformity of the duodenal bulb in its right proximal portion. With routine care the child became rapidly asymptomatic.

CASE 6.—S. C., a 4½ year old white girl, was seen on Jan. 19, 1942 with recurrent vomiting of two years' duration. The vomiting was unrelated to meals, and the child never complained of pain except for some periumbilical discomfort after vomiting. Anorexia had been present for the preceding three months, with a resultant loss of 3 pounds (1.4 Kg.) in weight. The physical examination revealed no abnormalities. A roentgenogram of the gastrointestinal tract showed the presence of a duodenal ulcer. A specimen of one of her stools gave a positive reaction for blood on one occasion. With routine care symptoms disappeared, and she was discharged on February 13 for further observation. A roentgenogram made just before her discharge showed no significant change in the duodenal lesion.

COMMENT

Regarding the general features of peptic ulcers in children, it is the experience of others that the younger group of children present the greater problem in diagnosis. In the prepuberal years the disease begins to conform to the adult pattern. It is the children of this age who tend also to be more noticeably underweight. The literature stresses the familial incidence of the disease, but in the cases reported on here the parent of only one child had a peptic ulcer and it was due to arteriosclerosis. Pain occurring with peptic ulcer in childhood is generally of long duration. In case 6, although the child was but 4½ years of age, symptoms had been present for two years. The typical night pain or prebreakfast pain is uncommon in the younger patients but will occur in the older group. This is likewise true of the symptomatic relief obtained by ingesting food or alkali. Pyrosis or acid eructations were not noted in any of the patients. Abdominal tenderness is more frequently epigastric in the older group and periumbilical in the younger group. It is generally agreed that the use of a gastric test meal is of little value in confirming or rejecting the diagnosis. It can be said, therefore, that diagnosis of peptic ulcer in childhood is basically a roentgenographic diagnosis. No doubt the frequency with which diagnosis is made will be directly proportionate to the frequency with which roentgenograms of the gastrointestinal tract are made in suspicious cases. The evidence on the roentgenogram of a child is no different from that of an adult. Borderline situations in interpretation will occur, in which the duodenal bulb may show irritability and irregularity without actual formation of craters. Where such changes

persist after the administration of atropine, the diagnosis of ulcer is presumptive. Such patients should receive routine therapy and periodic roentgen examinations.

The complications of peptic ulcer in childhood are laid especially to hemorrhage and pyloric obstruction. The occurrence of perforation is extremely uncommon. Hemorrhage can be severe, and fatal bleeding has been described. In general, the outlook for healing is excellent, and cure is obtained in the greater part of the cases from routine therapy with alkalis. Chronicity is not a particular feature of the disease in children, but when it occurs it presents the same therapeutic problem as that with the adult form of the disease. Subtotal gastrectomy may become necessary if the condition has become chronic or if intractable recurring bleeding occurs. The prognosis after operation has not been well established. It does not seem unreasonable to suppose that marginal gastrojejunal ulcers will occur after subtotal gastrectomy in children. This postoperative complication has been recorded as following simple posterior gastroenterostomy.

SUMMARY

A study of the problem of peptic ulcer in childhood was undertaken. The incidence, symptomatology, prognosis and therapy are discussed. Six cases are added to the others already recorded. The importance of roentgen examination of the gastrointestinal tract in demonstrating this disease as a cause of obscure abdominal symptoms in children is reemphasized.

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ICTERUS INDEX OF CORD BLOOD

THE GENESIS OF ICTERUS NEONATORUM

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In their early studies on icterus neonatorum Ylppö [1] and Hirsch [2] pointed out that bilirubin is usually present in increased amounts in cord blood. Subsequent investigators [3] have confirmed these observations. Ylppö also presented data showing that the intensity of the subsequent icterus—and the presence of visible jaundice—could be predicted from the height of the icteric index in cord blood. It is noteworthy that this observation of hyperbilirubinemia at birth has not been generally appreciated by pediatricians or obstetricians. Icterus neonatorum is generally assumed to develop only after birth, as a result of changes in the neonatal period.

A theory on the origin of icterus neonatorum was proposed by Schick [4] in 1921. He stated the belief that the fetal placenta played an important part in the breaking up of maternal hemoglobin during the latter months of pregnancy in order to make iron available for the creation of fetal hemoglobin (blood and muscle). Bilirubin appears as the iron-free part of the maternal hemoglobin and leads to hyperbilirubinemia. Icterus neonatorum is a continuation of this physiologic process, influenced by the normal changes at birth. The more intensive icterus of premature infants is explained by the assumption that they are

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1. Ylppö, A.: Icterus neonatorum (inc. I. N. gravis) und Gallenfarbsekretion beim Foetus und Neugeboren, Ztschr. f. Kinderh. **9**:208 (Dec.) 1913.

2. Hirsch, A.: Die physiologische Ikterusbereitschaft des Neugeborenen, Ztschr. f. Kinderh. **9**:196 (Dec.) 1913.

3. (*a*) Bonar, B.: The Icteric Index in the Newborn Infant, Am. J. Dis. Child. **50**:1143 (Nov.) 1935. (*b*) Weiner, S. B., and Reiner, M.: Icteric Index in the Newborn, Proc. Soc. Exper. Biol. & Med. **41**:83 (May) 1939. (*c*) Davidson, L. T.; Merritt, K. K., and Weech, A. A.: Hyperbilirubinemia in the Newborn, Am. J. Dis. Child. **61**:958 (May) 1941.

4. Schick, B.: Der Ikterus neonatorum eine Folge des Abbaues mütterlichen Blutes, Ztschr. f. Kinderh. **27**:231 (Jan.) 1921.

born when the placental iron metabolism is at its height. Overmature infants are relatively free of icterus because they are born when the metabolic exchange of iron has been completed.

Schick [4] called attention to the green border of the placenta of the dog, which is a zone of deposited biliverdin and bilirubin resulting from hemolysis of extravasated hemoglobin. This green border in the canine placenta is the equivalent of icterus neonatorum. The placenta is an organ essential in fetal blood formation, inasmuch as it is the only one capable of supplying iron to the growing organism. The bilirubin liberated during the destruction of maternal hemoglobin in the placenta is to some extent excreted into the intestine by the fetal liver, forming meconium. The meconium has been shown to be rich in biliverdin and bilirubin. Some of the liberated bilirubin may also be excreted through the maternal circulation. The observations of Wagner [5] and Williamson [6] on the amount of iron in the placentas of infants born in various stages of gestation are in agreement with this theory of the genesis of icterus neonatorum.

The efficiency of the fetal liver in excreting bilirubin has been a subject of much discussion, and its importance in icterus neonatorum has been considered by all investigators. The concept that jaundice due to a hemolytic process is always the result of inefficient excretion of bilirubin has been elaborated by Rich.[7] We feel, as Schick pointed out in his earlier studies, that the liver also plays an important role in icterus neonatorum.

Davidson, Merritt and Weech [3c] in 1941 contributed an excellent study of icterus neonatorum using an accurate microtechnic. They were able to confirm all the findings of Ylppö and Hirsch. They found a statistically significant association between the level of bilirubin in the cord blood and the intensity and duration of the hyperbilirubinemia in the infant. These investigators, in the light of their own studies and of pertinent findings of previous investigators, outlined a rational theory of the origin of icterus neonatorum. They stressed its early origin in fetal life and the relation between formation of blood and hepatic excretion of bilirubin. They believed the degree of icterus to be a measure of the functional maturity of the infant.

We tried to discover when the destruction of maternal hemoglobin would be most significant. It seemed probable that the greatest height

5. Wagner, R.: Icterus neonatorum und Eisengehalt der Placenta, Ztschr. f. Kinderh. **27**:251 (Jan.) 1921.

6. Williamson, A. C.: Placental Iron and Its Relationship to Icterus Neonatorum, Surg., Gynec. & Obst. **37**:57 (July) 1923.

7. Rich, A. R.: The Pathogenesis of the Forms of Jaundice, Bull. Johns Hopkins Hosp. **47**:338 (Dec.) 1930.

of bilirubinemia would be in the period of prematurity and that at the time of maturity and overmaturity of the baby there would be a decline in these values.

EXPERIMENTAL METHOD AND MATERIAL

The icteric index was studied in the cord blood of 141 normal newborn infants [8] in relation to their birth weight, total length and sitting height (crown to rump length). These measurements were used as indexes of maturity.

For the purposes of this study we have divided the infants into three groups according to their birth weights, as generally accepted in the pediatric and obstetric literature (table 1).

The blood was collected from the cut cord and the icteric index determined by the acetone method. We have previously pointed out the advantages of the acetone method and the fact that the icteric index obtained by the usual water method and that obtained by the acetone method are equal in serums of normal newborn infants.[9] The length and sitting height were accurately measured shortly after birth, and the child was weighed immediately after delivery.

TABLE 1.—*Generally Accepted Measurements of Maturity of the Newborn Infant*

	Weight, Gm.	Length, Cm.	Sitting Height, Cm.
Premature	Below 2,500	Below 45	Below 30
Normal	2,500 to 3,800	45 to 52	30 to 35
Overmature	Over 3,800	Over 52	Over 35

It is not within the province of this paper to enter into a discussion of the relative merits of the three measurements we have used in assessing maturity. We believe weight is the least accurate. Total length is a good measure according to most workers. We believe that measurements of sitting height are more accurate, since they allow for individual variations in length of the legs and therefore are somewhat superior to total length. We made no attempt to gather data on the menstrual history of the mother, inasmuch as these are notoriously subjective and inaccurate.

The designation of overmaturity is a generally debated one. We should prefer to consider the group of overmature infants merely as large infants who have had a long term intrauterine existence. They usually show, in addition to their larger size, better developed, thicker and whiter skin and appendages. They often resemble infants of 1 or 2 months of age in their appearance and general development. They usually laugh earlier.

8. The serum of an apparently normal infant has been excluded because his biliary metabolism seemed to be abnormal. The infant was born at term and weighed 3,570 Gm., with an icteric index of the cord blood of 36 units. On the third day of life he had a slight rise of temperature, and intense visible jaundice developed. The liver and spleen were not enlarged, and the stool and blood count were normal. The jaundice slowly subsided. This child probably had some hepatic disturbance.

9. Reiner, M., and Weiner, S. B.: Jaundice in Infants and Children: The Icteric Index as a Method of Determining the Type of Jaundice, Am. J. Dis. Child. **61**:752 (April) 1941. Weiner and Reiner.[3b]

RESULTS

Normal Group.—These infants weighed from 2,500 to 3,840 Gm. They had an average icteric index of 12.3 units. The range was from

TABLE 2.—*Distribution of the Icteric Indexes of the Various Groups of Infants*

	Total Number of Infants	Icteric Index		
		Above 12 Units	12 Units	Below 12 Units
Normal	88	36	14	38
Overmature	25	9	5	11
Premature	28	15	8	5

TABLE 3.—*Icteric Indexes of Eighty-Eight Normal Newborn Infants in Relation to Weight, Length and Sitting Height*

Icteric Index, Units	Sitting Height, Cm.	Length, Cm.	Weight, Gm.	Icteric Index, Units	Sitting Height, Cm.	Length, Cm.	Weight, Gm.
4	35	53	3,360	12	32.5	49	2,940
5	32.5	50.5	3,480	12	31	48	3,210
6	33	51	3,210	12	32	48.5	2,580
6	31	49.5	3,240	12	34	51	3,450
7	31	48	3,000	12	34	52.5	3,540
7	34.5	51	3,240	12	34	51.5	3,480
8	33	50	3,540	12	32	50.5	3,420
9	32	47.5	2,880	13	32.5	49.5	3,090
9	32	49.5	3,480	13	32.5	50.5	3,360
9	32.5	50	3,210	12	30	47	2,970
9	31.5	47	3,300	13	33.5	50.5	3,600
9	33.5	50.5	3,600	13	34	50.5	3,510
9	34	50.5	3,600	13	33	49.5	3,270
9	32.5	48	3,510	13	31.5	48	2,880
9	33	48	2,550	13	33	49	2,880
9	33	49.5	3,540	13	33	50	3,480
9	32	49.2	3,210	14	32	48	3,090
10	32.5	48.5	2,880	14	32	47	3,060
10	34	50.5	2,910	15	33.5	49.5	3,450
10	33.5	51	3,570	15	33	49	3,360
10	32.5	50.5	3,300	15	34.5	53	3,210
10	33	49.5	3,240	15	34	51.5	3,360
10	31	45.5	2,940	15	30	46	2,640
10	33	51	3,420	15	33	48	3,210
10	31	49	2,880	15	33.5	50	3,240
10	32	50.5	3,510	15	32.5	49.5	3,330
10	37	53	3,720	15	33	49	3,120
10	35	52	3,660	15	33	51	3,540
10	34	52	3,720	16	32.5	48.5	3,360
10	33	49	3,450	16	33	48.5	3,240
10	35	52	3,630	16	34	52	3,690
11	30	48	2,790	17	33	51	3,210
11	32	47	3,360	17	32.5	50.5	3,360
11	33	50	3,570	17	34	52	3,780
11	34	53	3,540	17	32.5	52.5	3,660
11	34	52	3.120	18	33	49.5	2,880
11	32	49.5	3,270	18	32	48	3,060
11	32.5	50	3,330	18	33.5	50	2,910
12	32.5	48.5	2,910	18	32.5	48.5	3,570
12	33	47.5	3,300	18	33	49	3,270
12	33.5	51	3,660	18	32	52.5	2,970
12	32	50	3,780	20	33.5	50	3,510
12	31.5	47.5	3,000	22	33	50.5	3,480
12	31	48	3,480	24	31	46.5	3,000

4 to 24 units. When one notes the considerable variation in size of these infants, it becomes apparent that the so-called full term infant represents considerable individual variation in growth and maturity. It is therefore easier to reconcile the rather wide variation in the values obtained in this group (table 3).

Overmature Group.—The 25 infants of this group weighed over 3,840 Gm. each. The average icteric index was 11.8 units. The variation was again wide, from 6 to 24 units. The distribution shows some tendency to lower values, approaching those obtained in later infancy under normal conditions (table 4).

TABLE 4.—*Icteric Indexes of Twenty-Five Overmature Infants in Relation to Weight, Length and Sitting Height*

Icteric Index, Units	Sitting Height, Cm.	Length, Cm.	Weight, Gm.	Icteric Index, Units	Sitting Height, Cm.	Length, Cm.	Weight, Gm.
6	34	51	3,885	12	33	50	4,110
6	34	52	4,500	12	32	48	3,930
7	36	52	4,140	12	35	51	4,080
7	40	56	4,630	13	31	49.5	3,840
7	35	54	3,930	13	32	49.5	4,290
8	34.5	52.5	4,410	15	34	53	4,020
9	37	55.5	5,070	15	33.5	53	4,380
9	36	54	4,770	15	35	52	3,870
9	34	54	4,500	15	37.5	53	4,470
10	38	53.5	5,280	16	36	52	4,320
11	33.5	51	3,930	18	37.5	55	4,230
12	35	52.5	4,080	24	36.5	54	4,140
12	35	53	4,620				

TABLE 5.—*Icteric Indexes of Twenty-Eight Premature Infants and Premature Twins in Relation to Weight, Height and Sitting Height*

Icteric Index, Units	Sitting Height, Cm.	Length, Cm.	Weight, Gm.	Icteric Index, Units	Sitting Height, Cm.	Length, Cm.	Weight, Gm.
9	29.5	46	2,310	14	31	46.5	2,430
10	28	43	2,430	14	18.5	41	960
10	30.5	48.5	2,130	15	27.5	43	1,500
11	31	47	2,500	15	29	45	2,400
11	28	45	2,160	15	30	47.2	2,550
12	30	46	2,040	15	29	47	2,340
12	28	45	2,340	15	29	46.5	2,250
12	27.5	42	1,920	15	29.5	45	2,460
12	28.5	45.5	2,130	16	30	46.5	2,160
12	31	46	2,400	17	26.5	41	1,800
12	27	42	1,770	19	28	43.5	2,220
12	30	45	2,130	20	20	40	1,620
12	27	42	1,770	24	28	45.2	2,220
13	26.5	38	1,080	24	28.8	45.3	2,400

Premature Group.—This group consisted of 20 premature infants and 4 sets of premature twins. They varied in weight from 960 to 2,500 Gm. The average icteric index of their cord bloods was 14.5 units. The variation was again from 9 to 24 units. Only five values were below the average of the group of normal infants (12 units). Within this small group of premature infants we could find no correlation between icteric index and weight, length or sitting height. We cannot state when hyperbilirubinemia in the fetus begins until a larger amount of data, especially on small premature infants, is assembled (table 5).

Evaluation.—Only 2 of the 141 infants had an icterus index of less than 6 units, which is considered the upper limit for normal adults and children.

These data were submitted to detailed statistical study in an attempt to detect any relationship and to evaluate the probability of any conclusions being the result of chance findings. We found no predictable relation between the icteric index of the cord blood and the weight, length or sitting height of any individual infant.

In comparing the groups of infants—especially the premature infants with higher icteric indexes and the overmature infants with lower indexes—the correlation factors are of debatable statistical significance. A considerably larger group of data would be necessary to permit one to draw any definitely significant conclusions (table 2). We feel that these data, however, bear out the clinical impression that premature infants and smaller babies are generally more icteric shortly after birth.

SUMMARY AND CONCLUSIONS

We have presented data on the icteric index of the cord blood in relation to the maturity of the normal newborn infant. Hyperbilirubinemia was present in 139 of 141 infants.

There is no predictable relationship between the icteric index of the cord blood and the birth weight, length or sitting height of any individual newborn infant.

As a group, premature infants show a tendency toward a somewhat higher icteric index, but the deviation from the random distribution is not large enough to warrant any definite conclusion from the comparatively small number of infants in this series.

We feel that the wide variation found within each group of infants is the expression of considerable individual differences in maturity, as well as the result of individual variation in blood volume, functional capacity of the liver, rate of formation and destruction of hemoglobin, degree of intrauterine anoxemia and intensity of placental metabolism.

The theories of the genesis of icterus neonatorum are reviewed. Our results are in agreement with those of Schick and Davidson, Merritt and Weech.

Miss Lena Sharney made the statistical analyses of these data.

17 East Eighty-Fourth Street.

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GONADOTROPINS AND LINEAR GROWTH

THE PITUITARY-GONADAL MECHANISM AND ITS RELATION TO LINEAR GROWTH AND SEXUAL DEVELOPMENT

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BROOKLYN

Since it is common knowledge that closure of the epiphyses and an accompanying cessation of normal growth occur under the influence of the interstitial cells of the sex glands (Falta and Meyer [1]), should it therefore be taken for granted that sexual development is inhibitory to linear growth and that sexual maturation and growth are antagonistic? For example, it has been stated by Engelbach and Schaefer that there is an antagonism between the sex and the growth factors elaborated by the anterior lobe of the pituitary gland.[2]

As can be seen, such problems bring with them not only such intriguing academic questions as what is the relationship and interrelationship of these glands but also, more specifically, such practical questions as whether therapeutic stimulation of the gonads of boys should be undertaken or whether such stimulation should be avoided because sex and growth factors are antagonistic and consequently premature closure of the epiphyses and termination of linear growth may be produced.[3]

In view of these questions, I am attempting in this report to give my conception, based on my past observations, of the growth-sex relationship that may exist in the pituitary-gonadal mechanism of the glandularly deranged boy and of some findings and conclusions on growth in such boys treated with chorionic gonadotropin.[4] I wish to

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Presented in part as "Growth and Sex Studies in the Male Child" on Dec. 18, 1940 before the Pediatric Section of the Medical Society of the County of Kings and Academy of Medicine of Brooklyn.

From the Endocrine Clinic of the Department of Pediatrics, New York University College of Medicine, and the Children's Medical Service of the Third Medical Division, Bellevue Hospital, Dr. Charles Hendee Smith, director.

1. Falta, W., and Meyer, M. K.: Endocrine Diseases, ed. 3, Philadelphia, P. Blakiston's Son & Co., 1923, p. 20.

2. Engelbach, W., and Schaefer, R. L.: Endocrine Dwarfism, Endocrinology **18**:387, 1934.

3. McCullagh, E. P., and McGurl, F. J.: The Effects of Testosterone Propionate on Epiphyseal Closure, Sodium and Chloride Balance and on Sperm Count, Endocrinology **26**:377 (March) 1940.

4. Dorff, G. B.: (*a*) Maldevelopment and Maldescent of the Testes: II. Further Observations on Treatment with the Anterior Pituitary-Like Gonadotropic Hormone, Am. J. Dis. Child. **50**:1429 (Dec.) 1935; (*b*) III. Treatment

(Footnotes continued on next page)

present briefly, as it is involved in this problem, my conception of the normal pattern of the pituitary-gonadal mechanism and its effects on the sex-growth relationship.

A perusal of the schematic chart (fig. 1) shows that in the normal pattern the anterior lobe of the pituitary gland secretes somatotropic and gonadotropic factors.

The purpose of the somatotropic, or growth, factor of the anterior lobe of the pituitary gland is, of course, to actuate and to maintain linear growth. It is logical, therefore, to assume that this gland will take such measures as are necessary to insure this growth. Primarily, it will keep the epiphyses open and will delay union; at the same time, it will furnish the stimulation necessary to cause an advance and a consequent development of ossifications.

The purpose of the gonadotropic, or sex, factor is to produce natural male hormone, androgen, by stimulating the interstitial cells of the

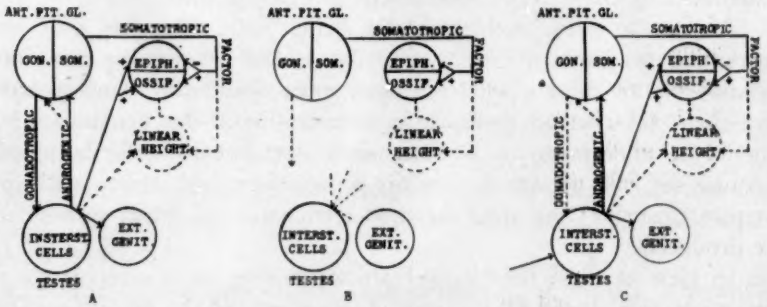

Fig. 1.—Schematic representation of the pituitary-gonodal mechanism as it affects the growth-sex relationship (*A*) in the normal person, (*B*) in a person with primary hypogonadism and (*C*) after chorionic gonadotropic therapy. The dotted lines indicate that although such an action may occur its modus operandi is not clear. The plus sign denotes the tendency to advance ossification and close the epiphyses; the minus sign denotes the tendency to keep the epiphyses open.

gonads. The androgen so produced not only stimulates the external genital apparatus but controls the growth initiated by the somatotropic

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of the Several Types of Adiposogenital Dystrophy in Boys, with Particular Reference to the Use of Gonadotropic Hormone from the Urine of Pregnant Women for Their Imperfectly Developed Genitals, J. Pediat. **8**:704 (June) 1936; (*c*) IV. The Treatment with Gonadotropic Hormone (Anterior Pituitary-Like) of Nonadipose Boys Showing Genital Dystrophy, ibid. **10**:517 (April) 1937; (*d*) Chorionic Gonadotropic Effects on Height and Osseous Development in Sexually Underdeveloped Young Boys, Endocrinology **27**:403 (Sept.) 1940; (*e*) Chorionic Gonadotropic Effects on Growth in Sexually Underdeveloped Older Boys, Am. J. Dis. Child. **60**:1043 (Nov.) 1940; (*f*) Gonadotropins and Growth: Rapid Growth in Height Produced by Chorionic Gonadotropin in a Dwarfed Infantile Identical Twin, J. Clin. Endocrinol. **1**:940 (Dec.) 1941.

factor of the anterior lobe of the pituitary gland by permitting and inducing an advance in ossifications, at the same time keeping growth within normal physiologic limits by causing closure of the epiphyses at the proper time. Stated simply, the purpose of the androgenic factor is to control growth, not to restrain or inhibit it.

In addition, androgen acts in a reciprocal capacity and under normal conditions produces a stimulative effect on the anterior lobe of the pituitary gland.

The harmonious balance between these factors helps to insure a normal pituitary-gonadal mechanism, necessary for a normal growth-sex relationship, and helps to maintain a normal and controlled increase of linear height.

Under abnormal conditions, it can be assumed obviously that production of these secretions has been disturbed and that the harmonious balance between the factors is being maintained no longer. This occurs in such persons as the so-called hypopituitary type (the dwarfed boy with sexual infantilism) and also in patients with macrogenitosomia praecox and in persons of the primary hypogonadal or eunuchoid type.

In the boy with so-called hypopituitarism seen in the clinic, when the primary deficiency is in the anterior portion of the pituitary gland there will be absence, or more likely a pronounced deficiency, of the gonadotropic and somatotropic factors. If this condition is recognized in childhood, I believe there will be present, in addition to the dwarfism, concomitant delay in the appearance of centers of ossification and epiphysial nuclei due to lack of the somatotropic factor; and if it extends into early adolescence, there will be present, in addition to the dwarfism, sexual infantilism and a delay in union of the epiphyses due to lack of the gonadotropic factor and androgen.

In macrogenitosomia praecox, the pathologic process is uncontrolled and severe, and as a consequence, I believe, an increased amount of androgen is produced. The intense stimulative effect of the excess androgen on the growth factor of the anterior lobe of the pituitary gland is probably the cause of the increase in height and of the rapid advance of ossification, while at the same time the intense stimulative effect of the androgen is the cause for the rapid and premature closure of the epiphyses. Thus, while there is an accelerated growth in height during childhood, stunting is the result when adulthood arrives, owing to the fact that the spurt of linear growth was relatively shortlived because of the premature closure of the epiphyses.

Thus far in this report, I have indicated that linear growth is dependent on the existence of a normally functioning anterior lobe of the pituitary gland that is producing growth and sex secretions in sufficient quantity and of potent quality. It is necessary, however, not only that these somatotropic and gonadotropic secretions exist in a

potent state but, as Smith has pointed out, that the tissues on which these secretions work be receptive to these specific charges or secretions and respond by their specialized action.[5] Thus one normally would expect the testicular tissue to be receptive to the charge from the sex, or gonadotropic, factor of the anterior lobe of the pituitary gland, and in turn one would expect it to respond by the production of an efficient androgen. One would also expect that the osseous system at its epiphysial junctions would be receptive both to the growth, or somatotropic, factor from the anterior lobe of the pituitary gland and to the androgenic secretion from the testes and respond by an orderly skeletal development.

On the other hand, I believe that the eunuchoidal boy or the boy with primary hypogonadism is an example of a person in whom the anterior lobe of the pituitary gland is functioning normally but whose gonads are nonreceptive to the gonadotropic charge from this organ. The explanation for the tallness of boys with deficient gonads differs somewhat from the explanation for the spurt in height produced in sexually deficient boys by means of chorionic gonadotropin. On the surface this would appear paradoxic. Generally, linear growth is produced by the somatotropic factor from the anterior lobe of the pituitary gland. In the boy with hypogonadism linear growth is frequently great, since it is relatively unrestrained because the gonads are nonreceptive to the gonadotropic factor of the anterior lobe of the pituitary gland and under the circumstances are not producing the androgen needed for its restraining influence on the somatotropic factor through its effect on the epiphyses. The epiphyses, lacking the needed stimulus, androgen, are prevented from closing and thus the brake which controls the growth secretions from a normal anterior pituitary gland is not present. With some variation in details, this explanation for hypogonadal tallness in general is the same as that expressed by Lisser and by other clinicians.[6] It is my belief that this type of condition is not dyspituitarism, as some clinicians are inclined to call it, but basically primary hypogonadism.[4b]

I am presenting a case of hypogonadism to emphasize some of the points in question.

A. P. at the age of 21 years was a sexually underdeveloped tall youth. He was 70½ inches (179.1 cm.) in height and 144 pounds (65.3 Kg.) in weight. He presented eunuchoid proportions; the lower measurement was about 8 inches (20 cm.) greater than the upper measurement. Although two small testes were resident in the scrotum, his entire genital apparatus was hypoplastic. His voice was high pitched. There was no growth of hair on his face; there was some hair in the axillas and sparse hair in the pubic region, which he says appeared after he had received some injections of gonadotropin at the age of 18 years. His epiphyses were widely open.

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5. Smith, P. E.: General Physiology of the Anterior Hypophysis, in Glandular Physiology and Therapy, Chicago, American Medical Association, 1935, p. 29.

6. Lisser, H.: Diseases of the Endocrine System, in Blumer, G.: Bedside Diagnosis, Philadelphia, W. B. Saunders Company, 1928, p. 71.

The use of chorionic gonadotropin was begun, and he received over 400,000 units in a period of twenty-two months. The response was surprisingly good. In addition, he received some testosterone[7] during the last few months of treatment.

At the end of twenty-two months, his testicles and phallus had increased strikingly in size; a good crop of pubic hair was produced; his voice had changed and facial hair had appeared, so that he began to shave. Furthermore, his height increased to 72¾ inches (184.8 cm.) and his weight to 192 pounds (87.1 Kg.), an accrual of 2¼ inches (5.7 cm.) in height and 48 pounds (21.8 Kg.) in weight (fig. 2). In addition, his epiphyses were almost united (fig. 3).

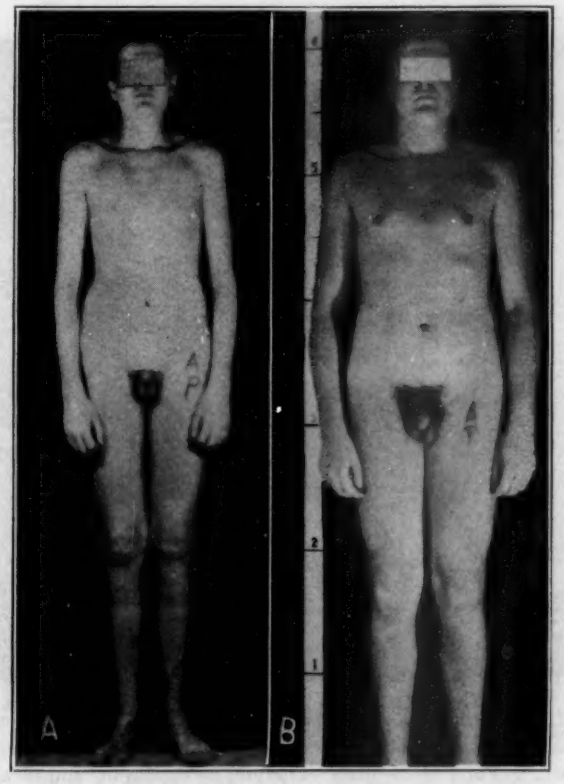

Fig. 2.—*A*, A. P. before treatment, at the age of 21 years. The height is 70½ inches (179 cm.) and the weight is 144 pounds (65.3 Kg.). Note the eunuchoid proportions.

B, A. P. after twenty-two months treatment with chorionic gonadotropin. The height is 72¾ inches (184.8 cm.); the weight is 192 pounds (87.1 Kg.). Note the genital development and the increase of 2¼ inches (5.7 cm.) in height and 48 pounds (21.8 Kg.) in weight.

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7. The chorionic gonadotropin (Pregnyl) and the testosterone propionate (Neo-Hombreol) were supplied by Dr. Leo Pirk, of Roche-Organon, Inc.

Here, then, is a youth of 21 years whose anterior lobe of the pituitary gland apparently was functioning normally, since tallness was present, but whose genital apparatus was underdeveloped because his gonads were not receptive to the gonadotropic charge from the anterior lobe of the pituitary gland—primary hypogonadism. As a consequence he lacked the androgen necessary to stabilize growth and therefore showed nonunion of the epiphyses even at the age of 21. Accelerated linear increase was maintained because a normally functioning anterior lobe of the pituitary gland produced sufficient somatotropic secretion and

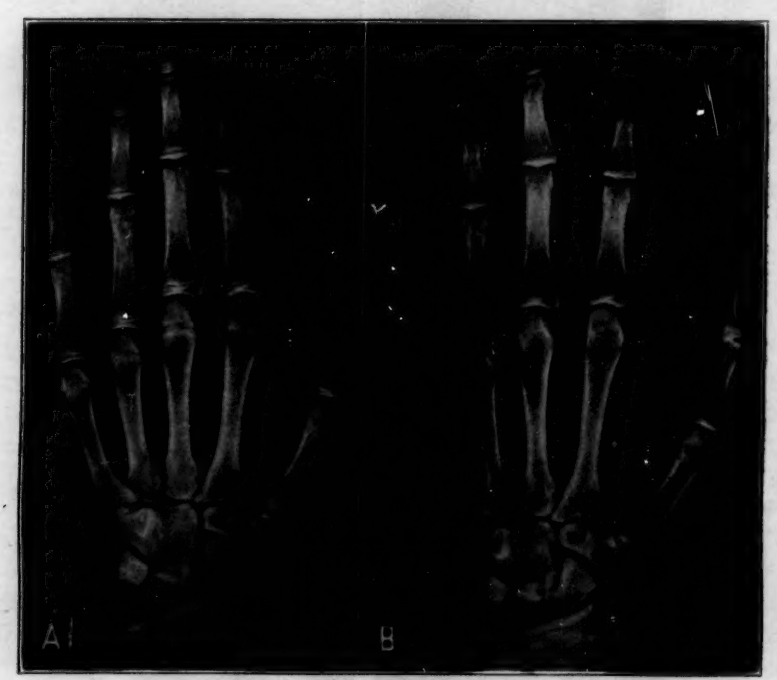

Fig. 3.—*A*, roentgenogram of the hand of A. P. at the age of 21 years, before treatment was instituted. Note the nonunion of the epiphyses of the metacarpal bones and phalanges and of the distal epiphyses of the radius and ulna. Note that the sesamoid bone of the thumb, which appears at about 13 years, is present but does not necessarily mean that puberty has begun.

B, roentgenogram of the same hand after twenty-two months' treatment with gonadotropin. Note the complete union of the epiphyses.

because androgen was lacking there was no great restraining influence on his growth in linear height. There was a great disproportion between the upper and lower measurements (8 inches [20 cm.]), a so-called eunuchoid proportion. I believe such a great disproportion is generally found in persons with primary hypogonadism and probably is due to the lack of androgen.

For reasons unknown, parenteral administration of chorionic gonadotropin acted as the key which unlocked the mechanism that permitted the gonads to become receptive to gonadotropin and to respond with the production of androgen. In this way a physiologically normal pituitary-gonadal relationship was established, and while gonadal development was taking place, linear height was also being increased (fig. 1 *B* and *C*). Eventually the desired union of the epiphyses took place.

It may be stated here parenthetically that although union of the epiphyses is delayed for many years in the untreated patients with severe primary hypogonadism, I have observed personally that the epiphyses in some such persons eventually close. I have seen in one such person nonunion at 26 years and closure of the epiphyses within a relatively short time after the institution of treatment with chorionic gonadotropin, and I have seen union in a 31 year old patient who had received no gonadotropic therapy. McCullagh and McGurl recently have demonstrated this occurrence by treating adult male hypogonadism with synthetic androgen (testosterone propionate).[5] It seems also that when the principal mechanism for closing the epiphyses is out of gear in these persons, eventually some other mechanism comes into play and finally closes the epiphyses. It is reasonable to assume that such an accessory mechanism does become active in the human economy, since it is known to occur after decerebration, etc. This secondary mechanism in hypogonadism is not believed to be in any way due to a gonadal effect. Furthermore, in some cases it may occur too late to be of much value in checking an acceleration of linear growth.

It is my contention, based on long observation, that androgen, a product of the interstitial cell produced by gonadal stimulation, can be considered as favoring growth. I believe this to be true because in my patients, as a rule, gonadal stimulation with chorionic gonadotropin produced increases in height concurrent with sexual development which were maintained over extended periods of time without causing epiphysial union prematurely.[4d, e] The case of A. P., already mentioned, may be considered by some an exception, since closure occurred during treatment.

Even in the case of A. P. the increase in height extended over twenty-two months of treatment before epiphysial union occurred, and it can be considered to have been maintained, since at the age of 23 years one would expect closed epiphyses. Yet, in spite of the relative tallness of this youth, 2¼ inches (5.7 cm.) was added to his height before epiphysial union occurred. This cannot be considered a sharp cessation of growth although such a cessation might have been expected in a person to whom gonadotropin was administered in such tremendous amounts (especially since some synthetic androgen was given for a few

months at end of the treatment [3]) and who was 22 years of age. Certainly such union in this instance cannot be considered as premature or to have been antagonistic to growth.

Some of the observations which I shall now list, in my opinion, suggest an alteration of the view that sexual maturity and growth are antagonistic.

In two recent reports [4d,e] I elucidated an observation, first reported in 1935,[4a] that by stimulating the gonads with chorionic gonadotropin in sexually underdeveloped boys there was produced a definite spurt of height in addition to sexual development.

More recently I confirmed this phenomenon in a well controlled set of dwarfed and infantile identical twins, one of whom at the age of 13 years after one year of treatment with chorionic gonadotropin gained 4 inches (10 cm.) in height, a gain over three times as rapid as was made by him in the same period prior to treatment and over three times that made by his untreated and controlled brother in the same period.[4f]

It is my belief that the administration of gonadotropic substance stimulated the interstitial cells of the testes to produce androgen; the androgen so produced supplied the link needed to reestablish the pituitary-gonadal reciprocal chain. In this way it acted, I believe, as a stimulant to the anterior lobe of the pituitary gland and caused it to produce further growth secretion. This supplemental growth secretion accounted for the spurt in linear growth, and this, together with the androgenic secretion, produced through gonadal stimulation, supplied the increased stimulus necessary to cause skeletal development and osseous advance.

Recently McCullagh and McGurl [8] indicated an osseous advance, and McCullagh and Rossmiller [8] and Brown and Ross [9] also indicated such an osseous advance and a spurt in height in clinical patients when synthetic androgen (testosterone propionate) was administered. The results obtained by these investigators with synthetic androgen confirmed my results with natural androgen, presumably attained through parenteral administration of chorionic gonadotropin. More recently Lurie and Hertzman [10] confirmed my original observations on the production of increased height and osseous advance in a group of sexually underdeveloped boys treated with chorionic gonadotropin.

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8. McCullagh, E. P., and Rossmiller, H. R.: Methyl Testosterone: III. Effect upon Body Weight and Growth, J. Clin. Endocrinol **1**:507 (June) 1941.

9. Brown, J. S. L., and Ross, A.: Influence of Testosterone Propionate on Cases of Retarded Growth, read at the Twenty-Fifth Annual Meeting of the Association for the Study of Internal Secretions, 1941.

10. Lurie, L. A:, and Hertzman, J.: Linear Growth and Epiphyseal Closure, J. Clin. Endocrinol. **1**:717 (Sept.) 1941.

I have since treated other patients with similar conditions and have achieved the same increases in height.

In all my boys, especially in the younger group, under 8 years of age, and this I believe to be of significance, follow-up examinations disclosed that even though there was produced an advance in ossification and in skeletal development, which in an occasional instance was brisk and caused apprehension, there was no evidence of impending union of the epiphyses nor any fear of a sudden termination of linear growth. Rather, ossification advanced and the epiphyses remained open and the new height levels were maintained with little variation in a goodly number of cases for many years after termination of treatment.[4d] There was some suggestion, though, in some of the older boys so treated that epiphysial union may occur a year or so ahead of time.[4e] It was my feeling that this would not affect the total final height to any great degree. For example, in one of my patients, whose case I am about to report more fully, after a follow-up of five years and only recently when he was 17½ years old, after an excellent height had been attained, I found signs of epiphysial union. Epiphysial closure at this point will modify his total height very little if it continues on this percentile line.

H. M., in March 1936, at the age of 11½ years, had bilateral undescended testes, which were fixed in the inguinal canals. He was a fairly alert and somewhat malnourished boy. His height was 54¾ inches (139 cm.); his weight was 62 pounds (28.1 Kg.). He was on the 40 percentile Burgess line (fig. 4).[12] He showed eunuchoid proportions. His osseous status was about that of a boy of 8 years—a delay of three and a half years. He was treated with an anterior pituitary extract containing the gonadotropic factor for a while, and then with chorionic gonadotropin. During a period of thirteen months of interrupted treatment he received about 82,000 units of chorionic gonadotropin. Consequently, both testes descended into the scrotum and the external genitals became rather well developed. During that same period his height was increased by 2¾ inches (7 cm.) and his weight by 13 pounds (5.9 Kg.). His ossification then was only about nine months retarded. His height curve reached the 50 percentile Burgess line, where it remained until he was 14 years old. At 14½ years, about two years after termination of treatment, his already accelerated curve was further accelerated spontaneously and reached the 60 percentile Burgess line. In March 1942, at the age of 17½ years, six years after the institution of therapy, the boy showed a fairly well developed body and an apparently normal genital apparatus. His height was 68¾ inches (174.6 cm.), and his weight was 123 pounds (55.8 Kg.). He was now on the 75 percentile Burgess height curve. In April 1940, at the age of 15 years 7 months, his epiphyses were still open. In April 1942, at the age of 17 years 7 months, the epiphyses of the hand had united, and those at the distal radius and ulna were

11. Footnote deleted by author.

12. Burgess, M. A.: The Construction of Two Height Charts, J. Am. Statist. A. **32**:290 (June) 1937.

almost completely closed.[13] There was present possibly a slight advance in his ossification above that normal for his chronologic age. His height was 69 inches (175.3 cm.), and his weight was 122 pounds (55.3 Kg.).

In a good many of my patients and in the boy whose case was just reported, synergistic effects of the gonads on linear growth was apparent during treatment and after treatment was terminated. Furthermore, once the effects of this pituitary-gonadal chain were established, it usually was maintained, apparently within physiologic limits, over a sufficiently long period and to indicate that termination of linear growth will not occur too prematurely and will not therefore become undesirable or possibly be considered as antagonistic. Nevertheless, one still will have to wait for the future to establish with any finality the benefits or disadvantages of such effects.

I believe that sexual development and growth are to be considered as antagonistic only in abnormal cases in which premature epiphysial closure ensues because of an existing pathologic condition wherein presumably there is elaborated too much androgen. This excess androgen is in part probably responsible for the rapid advance in ossification and eventually for the premature closure of the epiphyses. I am of course referring to the pathologic and uncontrollable picture of macrogenitosomia praecox.

In my patients treated with chorionic gonadotropin, there was very little to be feared at this time from a possible antagonistic effect. As I have indicated, some of my patients have been observed for many years and the beneficial effects of the therapeutically stimulated gonads on linear growth are apparent. In my opinion, one need not be too concerned about an immediate antagonistic effect and about premature epiphysial union if chorionic gonadotropin is administered judiciously as a therapeutic measure. It is obvious, however, that one should not at any time push this treatment to extremes or use it indiscriminately, especially for the very young child. In such a patient sexual precocity

13. At the age of 17 years and 7 months, this boy's epiphyses are practically closed and his bone status perhaps is slightly in advance of his chronologic age. There is very little, if any, room for further growth. It is my feeling that even if this boy does not increase in height for the next few years his percentile rank will be diminished only slightly, to about the 70 percentile curve, if carried to the age of 21 years. Even so, much has been accomplished, for when he was 11½ years old one did not know whether his height was to follow the 40 percentile curve or go to a lower curve, or whether he would ever reach a height on the 70 or 75 percentile line. The question whether therapy has accomplished the same end result in a slightly shorter period than would have been accomplished spontaneously in a longer period of time is difficult to answer, and any answer would be only conjectural. Suffice it to say that at 17 years and 7 months the youth is sexually well developed and is 5 feet 9 inches (175.3 cm.) tall, whereas originally it appeared as if he were destined to be short and perhaps to be sexually underdeveloped.

and a rapid advance in ossification may be produced, so that one may defeat the very purpose which one sets out to attain.

Finally, the effect of sexual development on linear growth in my patients treated with gonadotropin must be considered as synergistic, just as they should be considered synergistic during sexual maturation in the normal patient. In the normal person, I believe, it is only at the time when sexual maturation is thoroughly and wholly completed and all epiphyses have united that one can say that gonadal secretion is antagonistic to linear growth.

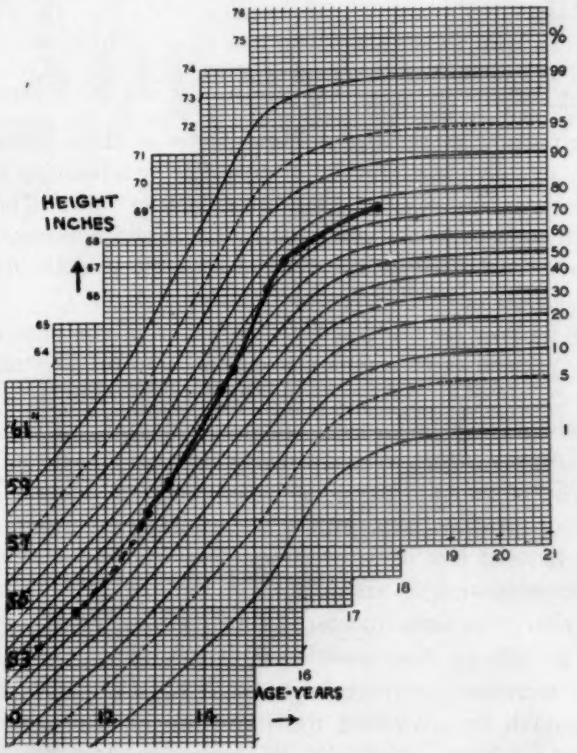

Fig. 4.—Height curve of H. M. recorded for six years on a Burgess growth chart.[10] The dotted line indicates the 13 month period of treatment with chorionic gonadotropin instituted at 11½ years. Note the progress from the 40 percentile to the 50 percentile curve during the period of treatment and the continuation of the height on this curve for the next year after treatment and the spontaneous progress of the height subsequently to the 75 percentile curve.[18]

SUMMARY AND CONCLUSIONS

Clinical observations made for the past decade and the impressions derived therefrom are presented in this report dealing with the pituitary-gonadal mechanism as it affects the interrelation of sexual and skeletal

development. Some of these reaffirm old conceptions; others, I believe, present new conceptions and offer suggestions for the revision of old ones, viz.:

1. There must be present a normal anterior lobe of the pituitary gland which elaborates somatotropic and gonadotropic secretion. The lack of both of these factors will cause the hypopituitary dwarf who shows infantilism.

2. The capacity of the tissues concerned with linear growth must be receptive to the specific hormonal charges and respond accordingly, thus maintaining an intact pituitary-gonadal chain; i.e., the gonads must react to gonadotropic stimulation of the anterior lobe of the pituitary gland, and the epiphysial junctions and ossifications must react to the somatotropic and to the androgenic secretions.

3. The purpose of the somatotropic factor of the anterior pituitary gland is to actuate linear growth. It does this by advancing ossification, yet at the same time it must keep the epiphyses open. The existence of a normal anterior lobe of the pituitary gland and nonreceptive gonads will produce the tall eunuchoid type of boy, the primary hypogonadal type, who shows delay in epiphysial closure.

4. The purpose of the gonadotropic factor of the anterior lobe of the pituitary gland is to stimulate the gonads to produce natural male hormone or androgen. Androgen causes an advance in the ossifications and controls growth by favoring epiphysial closure.

5. Androgen in turn reciprocates by having a tonic effect on the anterior lobe of the pituitary gland. It forms an integral link in the pituitary-gonadal chain concerned with normal linear growth. Stimulation of the anterior lobe of the pituitary gland by the androgen produced through stimulation with chorionic gonadotropin in boys with hypogonadism elaborates supplementary growth secretion and produces such spurts of growth as those mentioned in this report.

6. The secretion (androgen) produced by the gonads as a whole controls growth by advancing the formation of bone and eventually closing the epiphyses. Normally this secretion does not restrain or inhibit growth.

7. Sexual development is not antagonistic to linear growth in normal subjects; it is thought to favor it.

8. The period between the onset and the completion of sexual development is relatively long and allows for synergistic effects on linear growth before the so-called antagonistic effects set in and close the epiphyses. This is true not only in the person showing normal sexual development but in the one who is being treated successfully with chorionic gonadotropin for his sexual underdevelopment. Severe premature epiphysial closure in such persons has not been found to set in.

9. Too rapid and excessive production of androgen takes place in cases of macrogenitosomia praecox and, I believe, in turn causes the premature closure of the epiphyses.

10. The androgenic secretion provoked by the judicious use of chorionic gonadotropin is not to be feared as excessive and does not provoke premature closure of the epiphyses. I prefer the use of chorionic gonadotropin to synthetic androgen for stimulation of gonadal or skeletal development in children.

11. Sexual ripening or maturation, i.e. the end or completion of sexual development, in the normal person should imply epiphysial closure and termination of linear growth in addition to the complete development of the sexual apparatus. The converse is not necessarily true. Sexual development and growth become antagonistic only when sexual maturation sets in. As a rule this premature development is not desirable.

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CHANGES IN SIZE AND CONTOUR OF THORAX DURING FIRST POSTNATAL WEEK

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IOWA CITY

Morphologic and physiologic changes during the neonatal period are coming to constitute a nodal area of research. While the bulk of the literature on the human newborn infant has related to the loss in weight following birth,[1] investigation has also been made of such problems as changes in size of the uterus, weight of the adrenal glands,[2] capacity of the stomach [3] and calcium metabolism of bones [4] and teeth.[5]

It is the purpose of this paper to report a study on changes of the size and contour of the thorax during the first postnatal week. Specifically, attention will be given to (*a*) the absolute width and depth of the thorax and (*b*) the trend of change in thoracic shape expressed by the ratio chest depth $\times$ 100/chest width.

SUBJECTS

The subjects were 68 newborn white infants, 36 boys and 32 girls, obtained through the department of obstetrics and gynecology, University Hospitals, Iowa City. They represent a downward selection with respect to socioeconomic status, the mothers having been admitted as state patients.

Beginning Feb. 20, 1941, subjects were taken serially as birth occurred, except for the exclusion of infants considered premature, infants placed under special observation and infants physically deformed. The addition of subjects was continued until 75 were obtained. As many of the 75 infants as were available were reexamined on the fourth and eighth days. At the time of first examination, the infants ranged in postnatal age from 1 to 23 hours, with a mean of 8.1 hours. In weight at birth they varied from 2,580 to 4,730 Gm., with a mean of 3,473 Gm.

TECHNIC OF MEASUREMENT AND DEFINITIONS

Width of the Chest.—The instrument employed was a pair of wooden calipers. The infant was undressed and placed on the measuring table in the position of dorsal

From the Iowa Child Welfare Research Station, University of Iowa.
Dr. Howard V. Meredith made valuable criticisms.

1. Meredith, H. V., and Brown, A. W.: Growth in Body Weight During the First Ten Days of Postnatal Life, Human Biol. **11**:24-77, 1939.

2. Harris, J. A.; Jackson, C. M.; Paterson, D. G., and Scammon, R. E.: The Measurement of Man, Minneapolis, University of Minnesota Press, 1930.

3. Scammon, R. E., and Doyle, L. O.: Observations on the Capacity of the Stomach in the First Ten Days of Postnatal Life, Am. J. Dis. Child. **20**:516-538 (Dec.) 1920.

4. Sontag, L. W.: Evidences of Disturbed Prenatal and Neonatal Growth in Bones of Infants Aged One Month, Am. J. Dis. Child. **55**:1248-1256 (June) 1938.

5. Schour, I.: The Neonatal Line in the Enamel and Dentin of the Human Deciduous Teeth and First Permanent Molar, J. Am. Dent. A. **23**:1946-1955, 1936.

recumbency. At the time the measurement was taken, the arms and feet of the subject were in contact with the table. The arms were sufficiently abducted to permit passage of the instrument between their medial aspect and the lateral wall of the thorax, and the head was oriented so that a plane passing through the tragi and the orbitalia was at approximate right angles to the long axis of the body. The fixed branch of the calipers was applied lightly against the right lateral thoracic wall and the movable branch brought into light contact with the left wall. The reading was made at the level of the nipples with the branches of the calipers perpendicular to the table.

Depth of the Chest.—The instrument and the position of the infant were the same as for measuring chest width. The movable branch of the calipers was removed from the shaft, turned through 180 degrees and replaced. The fixed branch was then placed on the table with the shaft perpendicular to it and within 2 to 3 cm. of the lateral chest wall. The movable branch, now extended over the thorax, could be moved downward until it made light contact with the anterior wall of the chest at the level of the nipples. As in measuring width of the chest, readings were made to the nearest millimeter.

PROCEDURE

The experiment was designed for examination of each subject on the first, fourth and eighth postnatal days. For any given infant the procedure at each examination was as follows:

1. The infant was brought from the nursery to a private examining room, where all clothing except the standard naval dressing was removed.
2. Anthropometrist A placed the subject on the table and made his observations for width and depth of the chest. His readings were called off to an assistant, who handled all recording.
3. Anthropometrist B entered the room and after removing the infant from the table (in order to make the technic strictly independent throughout) duplicated the procedure followed by anthropometrist A.

In every instance I served as anthropometrist B. The records for anthropometrist A were taken by H. V. M. (79 per cent), E. J. M. (17 per cent) and V. B. K. (4 per cent).

No measurements were taken while the child was crying. In the case of a restless infant a given diameter was determined by making several readings. Every permanent record for a dimension was taken as the mean of the independent observations of two anthropometrists.

RELIABILITY OF THE MEASUREMENTS

The data obtained for the 68 infants on the first day were utilized in an analysis for reliability. For each thoracic diameter (*a*) the differences between the independent observations of anthropometrists A and B were distributed without regard to sign and (*b*) Pearson product-moment correlation coefficients were obtained from the absolute paired observations. The results were as follows:

Dimension	Number	Median Difference (Millimeters)	Number	Correlation Coefficient
Width of chest	68	1.25	68	.92
Depth of chest	68	1.14	68	.91

For both diameters approximately 90 per cent of the differences between the independent measurements of anthropometrists A and B did not exceed 3 mm. The maximum differences for width and depth of the chest were 5 and 6 mm. respectively.

RESULTS

In table 1 means are presented for width and depth of the thorax and for the thoracic index on the first, fourth and eighth postnatal days. Each mean index, shown in column 5, was computed from 68 individual indexes obtained by expressing anteroposterior diameter of the chest in per cent of the transverse diameter. Since no significant differences were found between the values for boys and for girls, the figures are reported for combined sex groups.

On the first day the individual values ranged from 9.2 to 11.8 cm. for width of chest, from 7.8 to 10.2 cm. for depth of chest and from

TABLE 1.—*Thoracic Diameters and Index on the First, Fourth, and Eighth Postnatal Days*

Age	Number	Mean Chest Width (Cm.)	Mean Chest Depth (Cm.)	Mean Thoracic Index *
First day (8.1 hours).....	68	10.50	8.94	85.2
Fourth day.....	68	10.34	8.53	82.6
Eighth day.....	68	10.38	8.67	83.6

* The thoracic index was obtained from the formula $\frac{\text{depth of chest} \times 100}{\text{width of chest}}$.

78.2 to 94.9 per cent for the thoracic index. Comparable minima and maxima for the eighth day were 9.2 and 11.4 cm. for width, 7.9 and 9.6 cm. for depth and 76.9 and 92.4 per cent for the index. The following facts are revealed by the table:

1. Both diameters showed decreases in mean size from the first to the fourth day. The drop of 4.1 mm. in depth was significant at the 1 per cent level, the value of t (the measure of significance)[5a] being 11.9. The drop in width (1.6 mm.) was also significant at the 1 per cent level, t being 3.33. It is "practically certain," therefore, that there was a true drop in both dimensions during the first four postnatal days. The amount of decrease, though significant in each instance, was slight.

2. The loss in depth between the first and the fourth day appeared with greater consistency in the individual records than did the drop in width. Only 5 of the 68 subjects failed to show drops in anteroposterior diameter, whereas with regard to the transverse diameter 25 subjects either remained stationary or showed slight gains.

5a. For a discussion of this method of estimating significance, see Fisher, R. A.: Statistical Methods for Research Workers, London, Oliver & Boyd, Ltd., 1928, chap. 5.

3. For the latter part of the first week the modifications in anteroposterior and in transverse diameter were somewhat dissimilar. There was a diminutive increase in width of the chest from the fourth to the eighth day, which lacked statistical significance (t equaled 1.1). Depth of the chest, however, appeared to have begun a definite trend of increase. The value of t was 4.21.

4. Examination of the values for the thoracic index revealed that on the first postnatal day the thorax of the infant was considerably wider than it was deep. In terms of percentage, depth approximated 85 per cent of width on the first day, 83 per cent on the fourth and 84 per cent on the eighth. The central 50 per cent of the indexes fell between 82.8 and 87.4 for the first day and between 81.2 and 86.1 for the eighth day.

TABLE 2.—*Results of Other Investigations of Width and Depth of Chest and Thoracic Index*

Investigator	Number	Mean Width of Chest (Cm.)	Mean Depth of Chest (Cm.)	Thoracic Index
Studies on the Living Newborn Infant				
Scammon and Rucker [6]				
15 min. after birth	23	7.7	8.2	106.0
First day (12 hours)	23	7.7	7.9	102.0
Third day	23	7.5	7.7	102.0
Fifth day	21	7.5	7.6	100.5
Seventh day	18	7.5	7.7	102.0
Freeman and Platt [7]				
First day	312	8.6	7.9	91.9
Eighth day	312	8.7	8.1	92.0
Studies on the Full Term Fetus				
Scammon and Calkins [8]	.....	10.2	8.8	86.3
Schultz [9]	.....	.....	.....	84.4
Rodes [10]	1	.....	.....	88.0

COMPARATIVE COMMENTS

For purposes of comparison table 2 was constructed to show the results obtained by other investigators both on full term fetuses and on living infants.

6. Scammon, R. E., and Rucker, W. H.: Changes in the Form and Dimensions of the Chest at Birth and in the Neonatal Period, Am. J. Dis. Child. **21**:552-564 (June) 1921.

7. Freeman, R. G., Jr., and Platt, V.: Skeletentwicklung und Wachstum der Säuglinge von der Geburt bis zu einem Monat, Anthrop. Anz. **9**:68-78, 1932.

8. Scammon, R. E., and Calkins, L. A.: The Development and Growth of the External Dimensions of the Human Body in the Fetal Period, Minneapolis, University of Minnesota Press, 1929.

9. Schultz, A. H.: Fetal Growth of Man and Other Primates, Quart. Rev. Biol. **1**:465-521, 1926.

10. Rodes, C. B.: The Thoracic Index in the Negro, Ztschr. f. Morphol. u. Anthropol. **9**:103-117, 1905-1906; cited in References on the Physical Growth and Development of the Normal Child, Publication 179, United States Department of Labor, Children's Bureau, 1927, p. 121.

The mean dimensions of the chest obtained in the investigation reported here exceed those of Scammon and Rucker by approximately 2 cm. in width and 1 cm. in depth. Unfortunately, the latter authors did not describe the anthropometric technic employed beyond stating that the measurements were made at the level of the nipples. (Their smaller mean for width of the chest obviously constitutes the major source of the higher thoracic index obtained by them.) The values of the present study are somewhat higher than those of Freeman and Platt and roughly identical with those obtained by Scammon and Calkins for full term fetuses.

The finding by Scammon and Rucker of a decline in the thoracic diameters during the first half of the first week is confirmed by the present study. However, the present study reveals a significant increase in depth of the chest during the latter half of the week, whereas both diameters were found by Scammon and Rucker to "decline slightly, remain stationary or show minor fluctuations probably without significance." [6] While in both these studies neither dimension had regained the initial loss by the end of the first week, values reported by Freeman and Platt for the first and the eighth day were practically equivalent.

Inspection of tables 1 and 2 reveals that the thoracic indexes of the present study approximated those obtained by Freeman and Platt from measurements of living newborn babies and those by Scammon and Calkins, Schultz and Rodes from full term fetuses. The indexes of Scammon and Rucker, however, indicated that the thorax is greater in depth than in width during the first postnatal week. According to these authors, six months or more of postnatal life pass before the thoracic index has "declined to the average which obtains just before birth." [6] They inferred that the rise in index obtained soon after birth was due to establishment of respiration.[11] The subsequent decline of the index was partially explained by the force of gravity on the anterior and posterior surfaces of the thorax, which, it was believed, would tend to decrease the anteroposterior diameter and to increase the transverse diameter.[12] Champneys' [13] research of 1881 was cited to show that the anterior surfaces and medial margins of the lungs expand before the

11. With the establishment of respiration there was claimed "a corresponding augmentation of the anteroposterior and transverse diameters of the chest." [8] Since for the close of the fetal period Scammon and Calkins [8] reported chest width and depth values of 10.2 and 8.8 cm. respectively, Scammon and Rucker's [6] means of 7.9 and 7.7 appear rather to support a decrease, which is both relatively and absolutely greater for width than for depth.

12. In this connection it may be noted that both diameters in their study showed a decrease.

13. Champneys, F. H.: Second Communication in Artificial Respiration in Still-Born Children: The Expansibility of the Various Parts of the Lungs, Med.-Chir. Tr., London **42**:87, 1881.

lateral portions and the inferior margins. The inference drawn was that "the changes in the form and dimensions of the chest in the neonatal period are reflected in the order and degree of expansion of the different parts of the lungs." [6] If Champneys' findings on the expansion of the lungs with the establishment of respiration are valid, they are not manifested in the changes of external thoracic size and shape during the first postnatal week obtained from the present investigation. Neither Freeman and Platt's figures nor those of this study confirm the assumption that the depth of the chest exceeds the width at the beginning of the neonatal period. Rather they lend support to the view that the thoracic index decreases uninterruptedly from the end of the fetal period to adulthood.[14]

SUMMARY

For the purpose of studying changes in the size and contour of the thorax during the first postnatal week, 68 newborn white infants were examined on the first, fourth and eighth days after birth.

Both width and depth of the chest were found to decrease during the first half of the first week. During the latter half of the first week, the transverse diameter failed to change significantly while the anteroposterior diameter showed a significant increase. At the end of the week neither dimension had fully recovered its initial loss.

The chest was shown to be appreciably greater in width than in depth throughout the experimental period. As expressed by the thoracic index, the depth was 85.2 per cent of the width on the first day and 83.6 per cent on the eighth day. These results do not support the conclusion that with the establishment of respiration the anteroposterior diameter of the thorax tends to exceed the transverse diameter.

Dr. Everett D. Plass and Dr. William F. Mengert, of the Department of Obstetrics and Gynecology, facilitated collection of the data.

Iowa Child Welfare Research Station, University of Iowa.

14. Meredith, H. V., and Knott, V. B.: Changes in Body Proportions During Infancy and the Preschool Years: I. The Thoracic Index, Child Development **8**: 173-190, 1937.

OSTEOMYELITIS OF THE LONG BONES IN THE NEWBORN

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There are few reports of osteomyelitis of the long bones in the newborn. Osteomyelitis of the jaw is not infrequent, and reviews have appeared by Bass,[1] Wilensky[2] and Poncher and Blayney.[3] Because this condition is uncommon and because it differs in course and prognosis from the form of the disease commonly seen in older children, we are reporting the cases of 4 patients from the Children's Medical Service of Bellevue Hospital.

Palew[4] in 1931 reported the case of a 2 week old infant with gonococcic osteomyelitis of the upper third of the left tibia. A local subcutaneous abscess which had formed was aspirated and later incised and drained. Complete recovery occurred, the drainage ceasing at the end of one week. The general health of the infant was good throughout the illness.

Dillehunt[5] reported on 3 infants with osteomyelitis, 2 of whom were newborn. One infant had staphylococcic osteomyelitis of the lower end of the right femur. This was treated by incision of a local subcutaneous abscess and opening of the periosteum, which was elevated by pus from within. The bone was not entered. The wound closed at the end of three weeks, and all evidence of the disease disappeared within five weeks. Another infant had streptococcic osteomyelitis of the left patella, which was treated by incision and drainage of a local subcutaneous abscess. Recovery was rapid, and all evidence of the inflammatory process subsided within four weeks. Dillehunt was impressed by the rapidity of resolution with simple drainage and the absence of subsequent destruction of bone and sequestration. He also

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1. Bass, M. H.: Acute Osteomyelitis of the Superior Maxilla in Young Infants, Am. J. Dis. Child. **35**:65 (Jan.) 1928.

2. Wilensky, A. O.: Pathogenesis and Treatment of Acute Osteomyelitis of Jaw in Nurslings and Infants, Am. J. Dis. Child. **43**:431 (Feb.) 1932.

3. Poncher, H. G., and Blayney, J. R.: Osteomyelitis of the Maxilla in Nurslings and in Infants, Am. J. Dis. Child. **48**:730 (Oct.) 1934

4. Palew, P.: Osteomyelitis of Gonococcal Origin in an Infant, Am. J. Surg. **13**:246 (Aug.) 1931.

5. Dillehunt, R. B.: Osteomyelitis in Infants, Surg., Gynec. & Obst. **61**:96 (July) 1935.

mentioned that the disease in infants is relatively benign; that the prognosis is favorable, and that spontaneous resolution without treatment may occur.

In 1935 Green [6] and again in 1936 Green and Shannon [7] emphasized the differences between osteomyelitis in infants under 2 years of age and the disease in older persons. In the infants the streptococcus was the etiologic organism in 63 per cent of the cases; in infants under the age of 6 months the mortality was 44 per cent; in the infants who recovered the wounds healed rapidly after operation, frequently in from four to six weeks; sequestration was infrequent; recurrences of the osteomyelitis were rare, and complete healing of the lesion in the bone was the rule. In many instances the site of the lesion could not be recognized in the roentgenograms taken in an end result study. Deformities were infrequent and when present were usually attributable to involvement of joints. The roentgenograms of infants differed from those of other patients in that subperiosteal new bone (involucrum) was visible much sooner than in older children; it usually involved half the length of the bone and suggested that sequestration of the shaft would occur, but this rarely happened. The healing process, as visible in the roentgenograms, likewise occurred much more rapidly than in older persons. In their treatment Green and Shannon gave primary consideration to the general condition of the child, not to the local lesion. If the infant survived the acute illness, the disease was brief and the prognosis of the osseous lesion excellent. Their procedure was to immobilize the affected part, apply poultices and give supportive treatment. Operation was not performed unless a palpable mass was present, and no procedure was carried out on the bone if the secondary abscess could be adequately drained. The wound was packed with petrolatum gauze and immobilized in plaster. It usually healed entirely in from four to eight weeks.

Cass [8] reported on 4 newborn babies with Staphylococcus aureus infection of the long bones. She also emphasized the benign character of the disease and the good prognosis if sepsis was not present. Her patients were treated by repeated aspiration of local subcutaneous abscesses, without open drainage. The results were good, and the lesions healed rapidly without sequestrum formation.

Osteomyelitis in the newborn child appears to be a benign disease; but when it is a manifestation of sepsis, the prognosis is more grave and

6. Green, W. T.: Osteomyelitis in Infancy, J. A. M. A. **105**:1835 (Dec. 7) 1935.

7. Green, W. T., and Shannon, J. G.: Osteomyelitis of Infants: A Disease Different from Osteomyelitis of Older Children, Arch. Surg. **32**:462 (March) 1936.

8. Cass, J. M.: Staphylococcus Aureus Infection of the Long Bones in the Newly Born, Arch. Dis. Childhood **15**:55 (March) 1940.

depends on the severity of the septic process. Fraser [9] reported on 30 newborn babies with umbilical sepsis which was complicated by metastatic foci of osteomyelitis. These were the most serious examples of acute osteomyelitis, and "a fatal result would appear to be almost inevitable." [9]

Dunham [10] described 39 newborn infants with septicemia, 4 of whom had osteomyelitis. Of these 4 patients, 3 died showing other manifestations of pyogenic sepsis. The sole recovery was in a male infant with osteomyelitis of the upper end of the right humerus and a Bacillus coli septicemia. Operation for the osteomyelitis was not performed.

Mount [11] reported on a 12 day old boy with hemolytic staphylococcic septicemia and osteomyelitis of the lower end of the left humerus. The child died after two days of illness.

REPORT OF CASES

CASE 1.—*Streptococcus viridans osteomyelitis of the left radius and suppurative arthritis of the left knee joint, with recovery.*

R. W., a boy, was delivered at Bellevue Hospital by cesarean section on Oct. 27, 1935. The weight at birth was 5 pounds 9 ounces (2,522 Gm.). The mother died of postoperative shock. The infant progressed normally for the first ten days after birth, and roentgenograms of the long bones taken on November 4 because of suspicion of syphilis were normal. On November 6 the child had diarrhea, vomiting and a temperature of 102.8 F. (39.3 C.). The diarrhea continued, and on November 19, at the age of 3 weeks, pitting edema of both hands and feet was observed. This subsequently subsided, and the temperature dropped to normal. On November 30, when the infant was 5 weeks old, the left knee was found to be red, swollen, hot and tender. Definite fluctuation was felt. The temperature was 99 F. (37.2 C.). The leukocyte count was 20,000. Aspiration of the swelling over the left knee yielded thick pus, culture of which showed Streptococcus viridans. The left knee joint was incised, and about 30 cc. of thick, foul pus was obtained. The edges of the wound were packed open with petrolatum gauze, but no drain was put into the joint. A roentgenogram taken on December 2 showed no abnormality of the bones forming the left knee joint; there was a pronounced swelling of the soft tissues.

On December 10, the left wrist was swollen, red and fluctuant. A roentgenogram (fig. 1*A*) showed an irregular area of rarefaction, involving the distal portion of the left radius. The temperature was normal. On December 12, an incision was made over this area, and 2 cc. of thick, green pus was obtained. Culture of this showed Str. viridans. The wound was packed with petrolatum gauze, and the wrist joint was immobilized.

By December 27, four weeks after the onset of illness, the wound in the wrist had practically healed. The wound in the knee continued to drain slightly until

9. Fraser, J.: Discussion on Acute Osteomyelitis, Brit. M. J. **2**:605 (Oct. 4) 1924.

10. Dunham, E. C.: Septicemia in the Newborn, Am. J. Dis. Child. **45**: 229 (Feb.) 1933.

11. Mount, W. B.: Septicemia in the Newborn, Am. J. Obst. & Gynec. **29**: 126 (Jan.) 1935.

Jan. 16, 1936. Because of limitation of motion of the left knee joint, which was held in 90 degree flexion, gentle traction was applied. A roentgenogram of the left knee taken on January 16 (fig. 1 *B*) showed periosteal raising over the lower half of the left femur. A roentgenogram of the left wrist taken on February 5 showed a diminution of the area of rarefaction previously present; there was also periosteal raising over the lower third of the left humerus. There was no sequestration. A roentgenogram taken on April 1, four months after the onset of illness, showed no abnormality of the long bones. However the child had limitation of motion of the left knee. Generally, he did well and gained weight. He was discharged at the age of 6 months, weighing 11 pounds 2 ounces (5,050 Gm.).

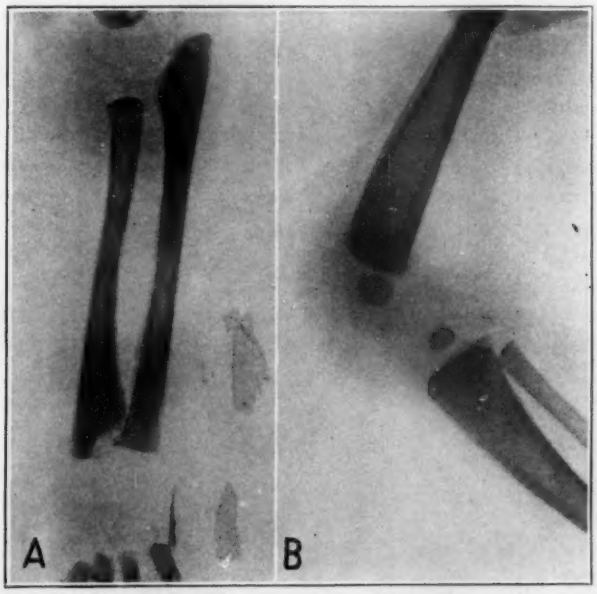

Fig. 1.—*A*, roentgenogram of the left forearm of R. W., 6 weeks old, showing an area of rarefaction in the distal portion of the left radius. *B*, roentgenogram of the left knee, taken at 11 weeks of age, showing swelling of the soft tissues around the knee and a rise of the periosteum over the lower half of the femur.

CASE 2.—*Staphylococcus aureus osteomyelitis of the left radius and left femur and suppurative arthritis of the left knee joint, with recovery.*

R. H., a boy, was born at Bellevue Hospital on Aug. 25, 1935. Delivery was spontaneous, and the birth weight was 7 pounds 14 ounces, (3,570 Gm.). The mother noticed that the baby had not moved his left arm since birth. On September 23, when he was 4 weeks of age, a swelling appeared over the left elbow and thigh. The child had seemed well since birth, although he had had a slight nasal discharge two weeks previously. He had eaten well, and the weight was 8 pounds 13 ounces (3,996 Gm.) at the age of 1 month. On his entry to the hospital the temperature was 100.6 F. (38.1 C.). The leukocyte count was 26,100, with 61 per cent polymorphonuclear cells. The red blood cell count was 3,110,000, and the hemoglobin content was 8.3 Gm. The left elbow, forearm and hand were swollen, warm and

moderately firm. There was a fluctuant area over the back of the left hand. The child did not move the left arm and leg. On September 27 the dorsum of the left wrist was aspirated and a small amount of pus was obtained, culture of which showed Staphylococcus aureus. Aspiration of the lower part of the left thigh gave 10 cc. of thick, greenish pus, which also showed Staphylococcus aureus on culture. A culture of the blood was sterile. Roentgenograms taken on September 25 (fig. 2 *A*

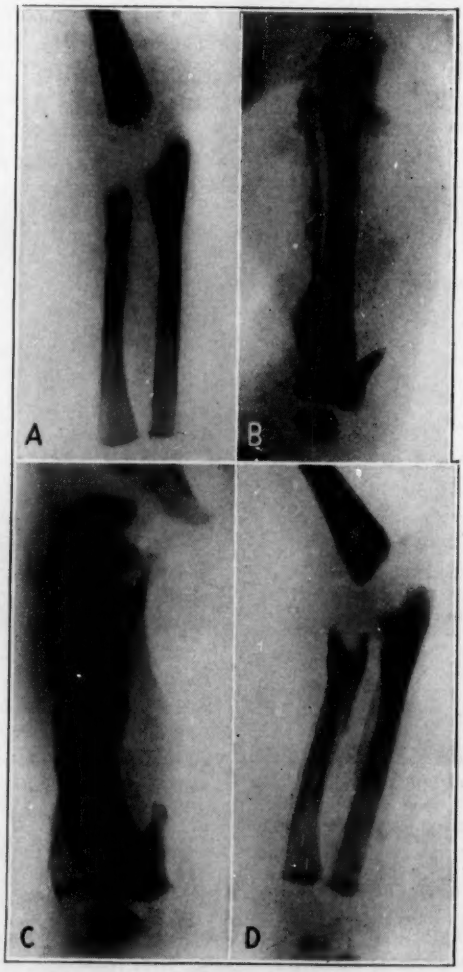

Fig. 2.—*A*, roentgenogram of the left arm of R. H., 4 weeks old, showing thickening of the periosteum over the lower half of the left humerus, rarefaction of the upper fourth of the left radius and thickening of the periosteum in this region. *B*, roentgenogram of the left thigh, showing the involucrum surrounding the left femur. There is rarefaction of the upper fourth of this bone, and a fracture is present in this region. A sharp spur extends upward from the external condyle. *C*, roentgenogram of the left thigh taken three weeks later, showing extensive involucrum formation around the femur. *D*, roentgenogram of the left arm taken at the same time as *C*, showing involucrum formation around the upper half of the radius.

and *B*) showed thickening of the periosteum over the lower half of the left humerus. The upper fourth of the left radius was rarefied, and the periosteum in this region was thickened. Surrounding the left femur was an irregularly outlined dense mass. A sharp spur extended upward from the outer condyle. There was rarefaction of the upper fourth of the left femur, and a fracture was present in this area. On September 28, an incision was made over the dorsum of the left wrist. A small amount of pus was obtained. An incision was also made over the lateral aspect of the left thigh down to the femur. A counterincision was made on the medial aspect of the thigh, and through and through drainage was obtained with rubber dam tissue. A large amount of pus was removed. The wounds were packed with petrolatum gauze. Posterior and lateral molded plaster splints were applied to the left thigh and leg and basswood splints to the left arm.

The child reacted well to these procedures. On October 4 the left knee joint was aspirated and pus was obtained. Bilateral incisions were made along the patella, and through and through drainage was instituted. Posterior and lateral molded splints were reapplied. The child continued to do well. On October 16, three weeks after the operation, the discharge from the wounds in the knee and wrist had ceased and the swellings in these regions had practically subsided. Roentgenograms taken at this time (fig. 2 *C* and *D*) showed extensive involucrum formation around the left femur and left radius. At no time did sequestration occur. The child was discharged on October 22, at the age of 3 months, weighing 9 pounds 12 ounces (4,422 Gm.). A follow-up roentgenogram taken seven months after the onset of illness showed complete healing of the involved bones, with some deformity of the lower part of the femur and the distal epiphysial center. The child was last seen in May 1941. At that time he was able to walk well, and there was good function of the left knee joint.

CASE 3.—*Staphylococcus aureus osteomyelitis of the proximal phalanx of the right fifth finger, with recovery.*

M. D., a boy, was born at another hospital on March 23, 1940. On the eighth day of life the mother noticed that the child cried a great deal after feeding. The next day a red swelling of the right fifth finger was seen. The child was admitted to Bellevue Hospital on April 7, at the age of 16 days. He had moderate edema of both eyes, both of which had a sanguinopurulent discharge. The conjunctivas were reddened. The right hand showed a pronounced swelling of the fifth finger; the skin between the fourth and fifth fingers was necrotic, and there was a foul-smelling discharge in this area. The child did not otherwise appear ill. The temperature was 99 F. (37.2 C.). The red blood cell count was 4,800,000, and the hemoglobin content was 11.5 Gm. The leukocyte count was 7,800, with 60 per cent polymorphonuclear cells. The blood culture was sterile. Culture of the discharge from the hand showed Staph. aureus. A roentgenogram of the right hand taken on April 8 showed no abnormal changes in the bones. On April 10 an incision was made over the dorsum of the right fifth finger and petrolatum gauze packing was loosely inserted. A small amount of pus was obtained, culture of which showed Staph. aureus. A tongue depressor splint was used to immobilize the finger. Meanwhile the temperature continued to be normal and the child gained weight. On April 26, administration of sulfathiazole, 0.1 Gm. every four

hours, was started and continued until May 3, a total of 4.0 Gm. having been given. A roentgenogram taken on May 1 (fig. 3) showed a rarefied area in the proximal phalanx of the right fifth finger. By May 29, seven weeks after the operation, the sinus had closed, and on June 3 the child was discharged, weighing 9 pounds 7 ounces (4,282 Gm.).

Fig. 3.—Roentgenogram of the right hand of M. D., 5 weeks old, showing the area of rarefaction in the proximal phalanx of the fifth finger.

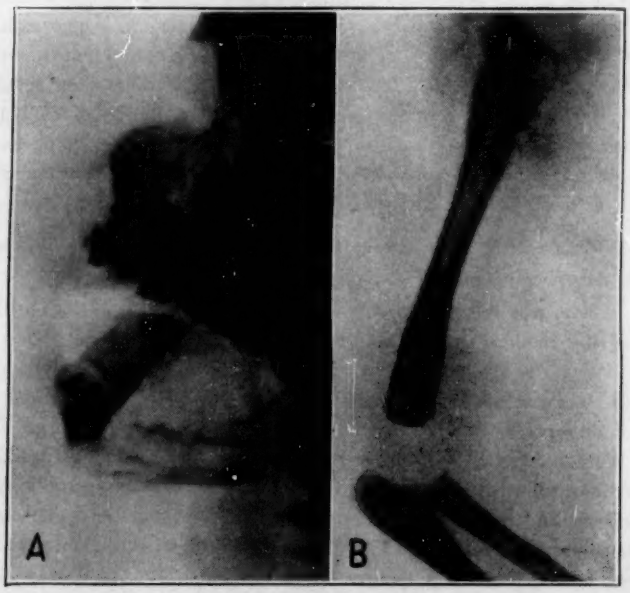

Fig. 4.—*A*, roentgenogram of a portion of the head of J. C., 4 weeks old, showing an area of rarefaction in the anterior portion of the mandible. Several of the tooth buds in the lower jaw are missing. *B*, roentgenogram of the right upper arm, showing periosteal thickening over the entire shaft of the humerus and an area of rarefaction in the upper portion.

CASE 4.—*Osteomyelitis of the mandible and Staphylococcus aureus osteomyelitis of the right humerus, with recovery.*

J. C., a boy, was born on Nov. 17, 1941 at another hospital. The delivery was spontaneous and uneventful. The child was apparently normal. The birth weight

was 9 pounds (4,086 Gm.). On the seventh day of life the temperature rose to 103 F. (39.4 C.). The white blood cell count at this time was 15,000. The temperature remained elevated, ranging between 101 and 103 F. (38.3 and 39.4 C.) daily for the next eight days. On the fourteenth day of life a swelling appeared over the gum on the left side of the lower jaw. The next day this swelling opened spontaneously, with drainage of purulent material and expulsion of both lower central incisor teeth. Within the next three days the two lower molars on the left were extruded. This area drained a purulent material. The temperature fell to normal. The child was discharged from the maternity hospital on December 12.

He was admitted to Bellevue Hospital on December 15, at 4 weeks of age, because the mother had noticed a swelling of both arms and inability of the child to move either arm. On admission the child did not appear ill. The weight was 8 pounds 6 ounces (3,800 Gm.). The temperature was 99 F. (37.2 C.). The white blood cell count was 11,200. There was a healing ulcerated area, about 5 mm. in diameter, in the lower anterior alveolar ridge in the midline. Both shoulders were swollen, the right more than the left. The skin over the right shoulder was reddened and showed a projecting, fluctuant mass on the inner surface. This was aspirated, and 2 cc. of thick pus was obtained. Culture showed Staph. aureus. Roentgenograms taken on December 17 (fig. 4 *A* and *B*) showed an area of erosion in the anterior portion of the left side of the mandible near the symphysis. Several of the tooth buds in the lower jaw were missing. There was swelling of the soft tissues around the left shoulder. There was also an extensive area of rarefaction involving the upper fourth of the right humerus, with periosteal thickening over the entire shaft of the humerus.

On December 23, at the age of 5 weeks, both shoulder areas were incised and drained. About 45 cc. of pus was obtained from the right shoulder and 60 cc. from the left. The wounds were packed lightly with petrolatum gauze, and the arms were immobilized by bandaging them to the trunk. Culture of the pus showed Staph. aureus. The temperature was normal throughout the entire stay in the hospital. The child took his feedings well and gained weight. By Jan. 2, 1942, ten days after operation, the discharge from the wounds had ceased and both incisions had healed. A roentgenogram taken on January 14 showed a diminution in the area of rarefaction over the upper fourth of the right humerus and an increase in the periosteal thickening. The child was discharged on January 16, weighing 9 pounds 6 ounces (4,254 Gm.). Neither sulfanilamide nor any of its derivatives was given to this child throughout his illness.

COMMENT

The striking feature of the cases reported here, as well of those reported by other observers, is the benign course of osteomyelitis of the long bones in the newborn. Characteristic are the quick healing of the osseous lesions, as observed in the roentgenograms, the rapidity of subperiosteal new bone formation, the short duration of discharge from sinuses and the quick healing of the operative wounds. In none of our patients did sequestration occur. This is in sharp contrast to the usual stormy and prolonged course seen in older children. None of our infants appeared acutely ill, and admission to the hospital was usually sought because of localized swellings of the extremities or

diminished motion of the arms and legs rather than because of severe systemic symptoms. The general condition of these infants remained good; they took their feedings well and gained weight. The operative procedures were limited to incision and drainage of palpable localized abscesses without involving the bone. All of this further confirms the experiences of Dillehunt, Green and Shannon, and Cass.

Green and Shannon ascribed the benign course of osteomyelitis in infants to the peculiar anatomy of the bone at this age. According to these authors, the vascular spaces of the bone are larger and the bone is of spongy texture and less rigid than in older children. In infants the cortical bone is particularly thin at the metaphysis. This construction allows freer communication between the marrow and subperiosteal spaces and thus provides a mechanism for decompression of pus from the metaphysis and marrow cavity to the subperiosteal spaces. The periosteum is more loosely attached in infants, and this further aids in decompression. Rupture of the periosteum, with decompression of pus, also makes for absence of gross sequestration. This and the facts that necrotic bone is rapidly absorbed in infants and that new bone is rapidly formed further contribute to the benign course and the good prognosis both for life and for eventual function of newborn infants with osteomyelitis of the long bones. The problem, as with osteomyelitis of older children, is to tide the patient over the period of bacteremia. The treatment of the osseous lesion is of secondary importance.

SUMMARY

Four newborn infants with osteomyelitis of the long bones, 3 of whom had involvement of more than one bone, are reported on. All of the infants recovered. The benign nature of the disease in this period of life when unassociated with severe sepsis is again stressed, and the good prognosis with the use of minor surgical procedures is emphasized.

Twenty-Sixth Street and First Avenue.

Case Reports

LEUKEMIA RESEMBLING CHLOROMA

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MONTCLAIR, N. J.

In 1823 a case of chloroma was first reported by Allan Burns. In 1893, on the basis of the blood picture, Dock [1] first pointed out the relationship of chloroma and leukemia, and in 1904 Dock and Warthin [2] definitely established this relationship. They defined chloroma as "a tumor-like hyperplasia of the parent-cells of the leucocytes, primary in the red marrow, the periosteum being involved only secondarily." Ewing [3] has further emphasized the tumor-like properties of the process by stating that "the chief significance of chloroma lies in the fact that it represents a leukemic process of a pronounced neoplastic type. The bulky tumors, the destructive local infiltrations, the distant heterotopic metastases, the atypical character of the cells and their very active proliferation provide all the essential features of a malignant neoplasm."

In 1930 Washburn [4] had collected 162 cases from the literature between 1923 and 1929. In 1937 Kandel [5] brought the number up to 175 proved cases at all ages by adding the more recent reports and omitting all those without biopsy or autopsy. In 1939 Atkinson [6] found that 130 cases had been reported in which the disease occurred in children under 14 years of age. A brief review of the literature by Washburn [7] between 1936 and 1940 has added 30 more.

Two main types of chloroma have been described: [8] that occurring in children, in which the chloromatous masses are the chief feature and

1. Dock, G.: Chloroma and Its Relation to Leukemia, Am. J. M. Sc. **106**: 152, 1893.

2. Dock, G., and Warthin, A. S.: A New Case of Chloroma with Leukemia with a Study of Cases Reported Since 1893, M. News **85**:971, 1025, 1078 and 1118, 1904.

3. Ewing, J.: Neoplastic Diseases, ed. 4, Philadelphia, W. B. Saunders Company, 1940, p. 401.

4. Washburn, A. H.: Chloroma: Report of a Case with Recovery Following Roentgenotherapy, with Review of the Literature, Am. J. Dis. Child. **39**:330 (Feb.) 1930.

5. Kandel, E. V.: Chloroma: A Review of the Literature from 1926 to 1936 and Report of Three Cases, Arch. Int. Med. **59**:691 (April) 1937.

6. Atkinson, F. R. B.: Chloroma in Children, Brit. J. Child. Dis. **58**:332, 1939.

7. Washburn, A. H.: Xanthoma or Chloroma: Follow-Up Data on Case of "Chloroma" Reported in 1930, Am. J. Dis. Child. **63**:335 (Feb.) 1942.

8. Kemp, T. A., and Williams, E. R.: Chloroma, Brit. J. Radiol. **14**:157, 1941.

the anemia is less pronounced, and that in adults, in which the anemia predominates. In children, the most common age is between 5 and 6 years and the duration is from one to eighteen months. The usual picture is that of a rapidly growing orbital tumor which results in exophthalmos or even proptosis. The cranium and dura are commonly affected, resulting in a pronounced enlargement of the head and a separation of the sutures. The bones may be involved,[9] chiefly the cranial bones, the ribs, the sternum and the long bones. The changes in the bones are seen mostly in the periosteum and the marrow, but there may be well defined destruction of the long bones. There are a generalized lymphadenopathy, a moderate enlargement of the spleen and liver and a progressive anemia. The anemia [2] is due to a diminished formation of red cells and not to hemolysis, as the marrow is replaced by leukocytes and tumor tissue. Rarely, there is hemorrhage from the mucous membranes and into the skin.[10] The patient has an irregular fever throughout the course of the disease. At autopsy there is seen to be a generalized infiltration of the abdominal organs by the tumor tissue. The tumor appears green on section, but the color fades on exposure to air. The green pigmentation is thought to be due to phagocytosis of the blood in the capillaries by the endothelial cells.

Only 2 instances of recovery have been reported: one by Lecène [11] of a patient in whom a tumor was excised from the humerus, and one by Washburn [4] of a patient in whom a tumor had been removed from the skull and who had had metastases to the tibia and femur.

The blood picture is that of an acute leukemia, with a white cell count anywhere up to 400,000 per cubic centimeter but usually around 50,000. Atkinson [6] reported that the number of lymphocytes is sometimes greatly increased (in 83 to 96 per cent of the cases), that myelocytes are usually few in number and that myeloblasts may be the only cells present. The predominating cells are described as large undifferentiated mononuclear cells, designated as large lymphocytes, myelocytes or mixed forms. No case of small cell lymphatic leukemia has been reported. In the case reported by Roehm, Riker and Olsen [12] the patient had a fairly normal differential count. A few cases of

9. Doub, H. P., and Hartman, F. W.: Lymphocytic, Myelocytic and Monocytic Neoplasms: Roentgen Diagnosis and Treatment, J. A. M. A. **105**:942 (Sept. 21) 1935.

10. Swanson, L. A.: Aleukemic, Myelogenous Chloroma, Am. J. Dis. Child. **44**: 140 (July) 1932. Jones, I. G.: A Case of Chloroma, Lancet **2**:246, 1939.

11. Lecène, M. P.: A Case of Chloroma of the Upper End of the Humerus, Treated by Resection: Healing Maintained at the End of Eleven Months, Bull. et mém. Soc. nat. de chir. **53**:1328, 1927.

12. Roehm, H. R.; Riker, A., and Olsen, R. E.: Chloroma: Report of a Case, Ann. Int. Med. **10**:1054, 1937.

aleukemic chloroma have been described. Brannan [13] stated the belief that aleukemic stages of chloroma are common, whereas proved true aleukemic forms of the disease are very rare. There is an accompanying anemia of varying degree, with anisocytosis and poikilocytosis and normoblastosis.

There has been a difference of opinion as to the type of the predominating cell. Before 1920 most of the cases were reported as instances of lymphoid leukemia, but since that date the general belief is that these are all cases of myeloid leukemia. Kandel [5] has made the most recent complete survey of the literature and has summarized the opinions of the chief authorities. Brannan,[13] Burgess,[14] Washburn,[4] Kemp and Williams,[8] and Askanazy [15] expressed the belief that the leukemia is always of myeloid origin. The textbooks differ among themselves, but Ewing [3] and Delafield and Prudden [16] have described both lymphoid and myeloid forms. In 1937, reporting chloroma in a 13 year old girl, Roehm, Riker and Olsen [12] stated that they "believe the case can not be classified as either lymphatic or myelogenous in origin as the tumor cell is a primitive blast which might conceivably differentiate into either a lymphocyte or a myelocyte." The oxidase test, by which dark blue granules of cytoplasm are manifested in myelogenous cells, is used to distinguish the two types, but the result is not always satisfactory. The test is useless in differentiating between lymphoblasts and myeloblasts, as neither cell has granules.

The following case of leukemia is reported as one in which the patient had the clinical features of chloroma, especially the typical chloromatous facies, although it cannot be definitely classed as such since autopsy or biopsy was not done. The large monocytes seen in the stained blood smears were lymphoblasts. There were no metastases to bone. However, Cohen [17] has reported a case of chloroma in which the only change revealed by roentgen examination was a separation of the bones of the skull.

REPORT OF A CASE

A 2½ year old white boy of Italian parentage was first seen in the outpatient department of Mountainside Hospital, Montclair, N. J. on Oct. 3, 1941. The father stated that for several weeks the child's eyes had appeared swollen, although they

13. Brannan, D.: Chloroma: The Recent Literature and a Case Report, Bull. Johns Hopkins Hosp. **38**:189, 1926.

14. Burgess, A. M.: Chloroma, J. M. Research **22**:133, 1912-1913.

15. Askanazy, M.: Personal Researches on the Nature of Chloromata, Internat. Clin. **1**:67, 1917.

16. Delafield, F., and Prudden, T. M.: Text-Book of Pathology, revised by F. C. Wood, ed. 16, Baltimore, William Wood & Company, 1936, p. 547.

17. Cohen, M.: A Case of Chloroma with Ocular Lesions, Arch. Ophth. **57**: 238 (May) 1928.

did not seem to be painful, and that he had been less active than usual. There were no other complaints.

The child was well developed and well nourished, somewhat apathetic and fretful. His skin was pale; his head was of normal size, and there was a slight though definite periorbital swelling. The pupils reacted normally. His tongue was

Fig. 1.—Photograph of the patient.

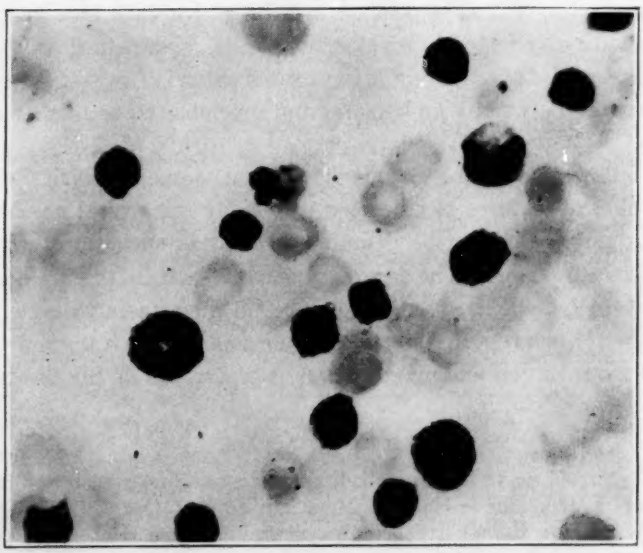

Fig. 2.—Photomicrograph of a stained blood smear.

somewhat thickened and protruded slightly. There were numerous enlarged submaxillary nodes, the size of peas, freely movable and not tender, and a few shotty inguinal nodes. His throat was normal; his lungs were clear, and in other respects also the results of his physical examination were normal. He was given a tuberculin patch test and referred for a complete blood count and urinalysis.

The following week he returned to the clinic. At that time he was coughing and his respirations were rapid and somewhat labored. The nodes in his neck had

increased in size, and there were a few palpable nodes in the left axilla. There was a widened area of dulness on both sides of the dorsal vertebrae, and a few scattered moist rales were heard throughout his lungs. The swelling of his lids and below

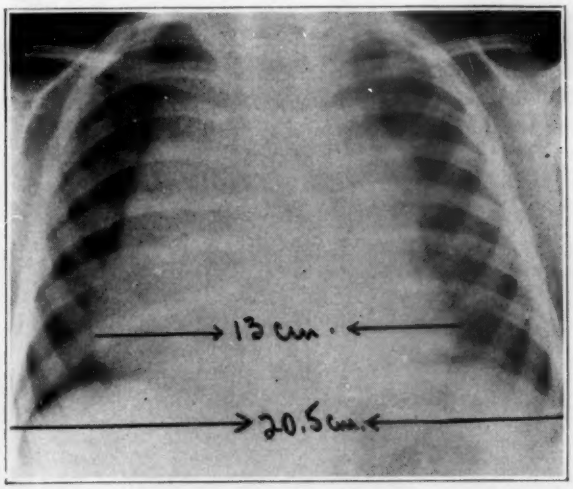

Fig. 3.—Roentgenogram of the chest of the patient, showing the pronounced widening of the mediastinal shadow.

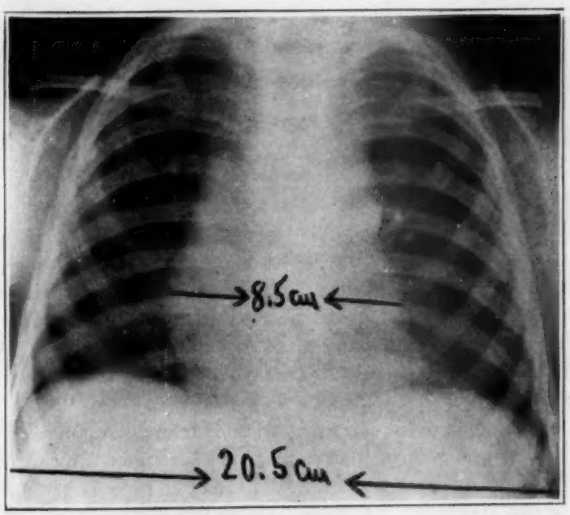

Fig. 4.—Roentgenogram of the chest, showing the reduction in width of the mediastinal shadow after roentgen therapy.

his eyes had increased. His spleen was felt 1 fingerbreadth below the left costal margin, firm and not tender. His liver was felt to be firm and enlarged 2 fingerbreadths below the right costal margin. Urinalysis showed a trace of albumin.

His hemoglobin content was 12 Gm.; his red cell count, 3,630,000 per cubic millimeter, and his white cell count 15,000, with 2 per cent polymorphonuclears and 98 per cent lymphocytes.

He was admitted to the hospital, and another examination showed: hemoglobin, 6.4 Gm.; red cells, 2,510,000, and white cells, 173,000, with 1 per cent polymorphonuclears and 99 per cent large and small lymphocytes. Two days later, his anemia had progressed still further; the hemoglobin content was now 5.8 Gm., the red cell count 2,270,000 and the white cell count 156,000, with the same differential count. He was given five small transfusions of citrated blood over a period of a week, totaling 685 cc. His blood count improved promptly: The hemoglobin content increased to 9.4 Gm., the red cell count to 4,000,000, and the white cell count to 67,600, with 4 per cent polymorphonuclears and 96 per cent lymphocytes. However, the improvement was only temporary, and two weeks later the values had dropped back to hemoglobin 6.4 Gm., red cells 2,690,000 and white cells 211,000, with only lymphocytes in the differential count. His platelets numbered 160,000, and his bleeding time was four minutes and twenty seconds.

Fig. 5.—Photograph of the patient two weeks after his admission to the hospital

The examination of his stained blood smears showed that the red cells were pale; there were pronounced anisocytosis and poikilocytosis, and a few nucleated red blood cells were seen in each slide. The white cells showed 70 per cent large mononuclears and 30 per cent small lymphocytes. The cells reported as large mononuclears were larger than polymorphonuclear cells. They had large, irregular nuclei, which contained nucleoli, and were probably lymphoblasts. A few basket cells and eosinophils were seen, but no myelocytes. The oxidase test for distinguishing granules was not done.

Roentgen examination of his chest showed an extreme widening of the mediastinal shadow. Roentgenograms of his extremities showed nothing unusual except healed rickets. He was given roentgen therapy, a total of 200 r over the anterior portion of his chest in two treatments. A week later he received a 200 r dose to the right side of his neck, and three days later, a similar dose to the left side. A week after roentgen therapy, there was a 20 per cent reduction in the size of the mediastinal mass, and two weeks later there was no evidence of any mediastinal enlargement. By that time his cough had ceased. After each treatment he was noticeably dyspneic for several hours.

After two weeks in the hospital, it was noticed that his head was increasing in size. A roentgenogram of his skull showed that there was some increase in the convolutional markings due to increased intracranial pressure. All sutures were considerably separated. The sella turcica and clinoid processes appeared normal. There were no sign of bone metastases. Another roentgenogram of his skull a month later showed the same widening of the sutures, especially the frontoparietal and sagittal sutures, but no metastases.

There was a gradual but noticeable increase in the exophthalmos, with edema and ecchymosis of the lids and below the eyes. Examination of the eyegrounds showed slight hyperemia of the disks but no evidence of papilledema. The nodes of his neck, axilla and groin continued to enlarge. There were no hemorrhages from mucous membranes or into the skin. The liver and spleen became further

Fig. 6.—Roentgenogram of the skull, showing the widening of the sutures and the absence of metastases.

enlarged, down nearly to the umbilicus. He had a low grade fever, with temperatures varying from 99 to 101.5 F., and his pulse rate was slightly elevated, between 100 and 130 beats per minute.

Blood counts done at frequent intervals showed an increasing anemia and a rise in the number of white cells. The last examination, done two weeks before death, showed hemoglobin 3.2 Gm., red cells 1,380,000 per cubic millimeter and white cells 270,000, with the same sort of differential count as before, only lymphocytes and lymphoblasts. A sternal marrow puncture was done, and the stained smear showed much the same picture as the blood, large and small lymphocytes and lymphoblasts.

The child gradually became weaker, was taken out of the hospital by the parents and died at home on December 31, less than three months from his first visit to the clinic. Permission for autopsy was not granted.

SUMMARY

A case of lymphatic leukemia with the clinical appearance of chloroma in a 2½ year old boy is reported. He had an enlarged head, with wide separation of the sutures, pronounced exophthalmos and enlarged lymph nodes, especially of the neck and mediastinum, but no metastases to bone. The predominating white blood cell was a lymphoblast, and no myelocytes or myeloblasts were seen.

71 Myrtle Avenue.

HUMAN DOUBLE MONSTER (SO-CALLED SIAMESE TWINS)

AN ANATOMIC PRESENTATION

BERNARD MORTIMER, M.D., PH.D.
AND
JACK D. KIRSHBAUM, M.D.
CHICAGO

In less than a year there have been 2 double monsters born at the Cook County Hospital. The first, reported elsewhere (fig. 1),[1] was the second double monster in 82,000 deliveries since 1905, and the present is the third in approximately 85,000 deliveries since that date.

REPORT OF A CASE

Mrs. R. P., a Negro woman of 20 years, pregnant for the first time, had her last normal menstrual period on Aug. 27, 1940, which made her due date approximately June 4, 1941. In the antepartum clinic her blood pressure was normal; her Kahn reaction was negative; a smear for gonococci did not show the organisms, and her urine was free of albumin. She entered the hospital at 7:25 a.m. on April 20, stating that the bag of waters had ruptured. She was having moderate pain.

Physical examination on entrance revealed edema of both ankles, blood pressure of 170 systolic and 92 diastolic and albumin in the urine (2 plus). Rectal examination showed cervical dilatation of about 3 to 4 cm. and a prolapsed extremity, which on sterile vaginal examination was found to be a foot with the pulsating cord lying alongside. The patient was given a hypertonic solution of dextrose with magnesium sulfate intravenously and put in the Trendelenburg position. When the pulsations of the cord could not longer be felt, extraction of the fetus was begun. This was difficult, and the cervix was incised at the level of 10 o'clock and 3 o'clock to remove the cervical dystocia. When a third lower extremity (fused) was born, the true nature of the dystocia was exposed, and a complete reexamination was made. This revealed a double monster, fused from the pelvis to the shoulder girdle.

Embryotomy was the delivery of choice. Decapitation and amputation of the fused upper extremity were done, and the monster was delivered. The placenta was removed manually.

Puerperal endometritis developed but rapidly subsided under treatment. The patient left the hospital on the eleventh postpartum day.

From the Department of Pathology and the Department of Obstetrics, Cook County Hospital.

1. Mortimer, B.; Kirshbaum, J. D., and Fields, J. E.: Human Thoracopagus Monster (So-Called Siamese Twins), Am. J. Obst. & Gynec. **42**:132-136 (July) 1941.

Fig. 1.—Male twins fused from sternum to the umbilicus (true thoracopagus monster).

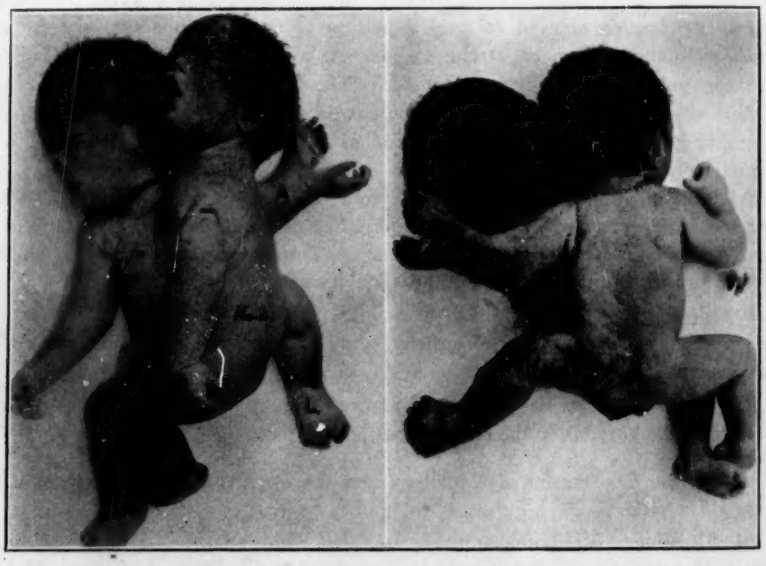

Fig. 2.—Anterior and posterior views of fused female twins, showing fusion of the arms (*A*) and legs (*L*).

Necropsy (Performed by J. D. Kirshbaum).—The general form and contour of the monster are shown in figure 2. The twins were girls, weighing 3,160 Gm. together; the longer (twin 2) was 39.5 cm. long, and the shorter twin (1) was 37 cm. The roentgenogram (fig. 3) shows the relation of the skeletal structures: the bony fusion from shoulder girdle to pelvis, with complete and separate spines; the fusion of the soft tissues of two of the upper extremities, with complete and separate bony structures; the common lower extremity, with the fused femurs in a single socket; the fused tibias; the separate fibulas, and a common great toe. The external genitalia consisted of a common vulva, divided in the center to form two vaginal orifices. There were two urethral orifices. The single anus was imperforated, only a dimple showing.

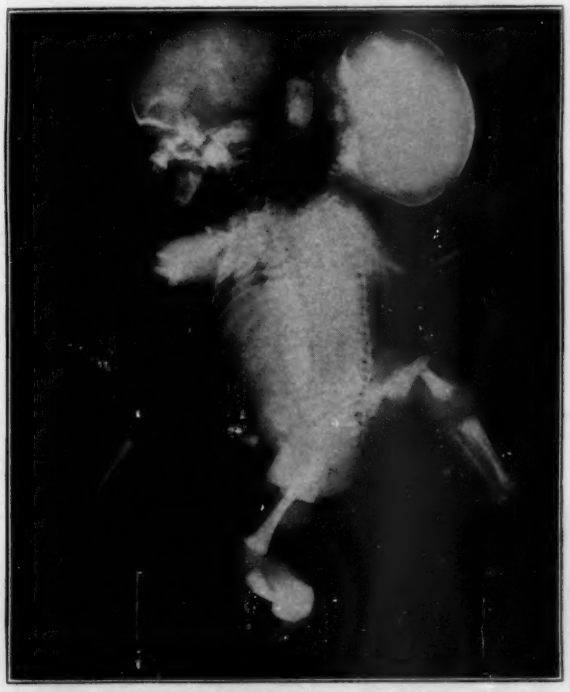

Fig. 3.—Roentgenogram of the skeletal structures, showing traumatic fracture of the common fused femur, fused tibias and a common great toe.

The line of fusion of the twins started at the shoulder girdle and continued to the perineum. Each fetus had only one nipple. There was only one umbilicus, with a single umbilical cord. The anterior line of fusion began a little beyond the midline of each twin and extended to the midaxillary line, all layers of tissue being involved. The fusion of the upper extremity involved only soft parts, but in the lower extremity the femurs were fused, fitting into a common acetabulum; there were separate fibulas, fused tibias and a common great toe.

The sternums were fused along one lateral margin from the manubrium to the xiphoid process, with resulting fusion of the ends of the ribs on that side; thus a common thoracic cavity was formed. The two diaphragms were fused at the level of the sixth ribs.

A single fused thymus gland was present. There was a common pericardial sac, containing two complete four-chambered hearts (fig. 4). In the center of the sac in the superior portion, there was a septum extending for 20 mm. downward along the line of fusion of the two sacs. In the inferior margin there was a fenestrated membrane which extended upward for 11 mm. The hearts were mirror images of each other, the heart of twin 1 having failed to rotate. Each heart had a widely patent ductus arteriosus. The aorta of the heart of

Fig. 4.—Photograph of the excised viscera, showing thymus (*T*), pericardial sac (*P*), hearts (H_1 and H_2), lungs (*Lu*), common fused liver (*L*), spleen (*S*), kidney (*K*), dilated sigmoid colon (*C*) and greatly dilated rectum (*R*).

twin 1 was in the same plane and to the right of the pulmonary artery, while in the heart of twin 2 these vessels occupied their normal positions.

There were two separate respiratory systems; the lungs of twin 2 were normal, but in its mate each lung contained two lobes, there being only a slight separation of the upper and middle lobes of the right lung.

The livers were fused, but each twin had its own gallbladder and bile duct system (fig. 5). The gastrointestinal tracts were separate to their fusion, 66 cm. from the ligament of Treitz, forming a common ileum, colon and rectum.

There was only one appendix. There was a marked dilatation of the rectum from the rectosigmoid junction to the imperforate anus (fig. 5). The spleens and pancreases were normal. Each twin had a complete and grossly normal urinary system. The adrenal glands were normal.

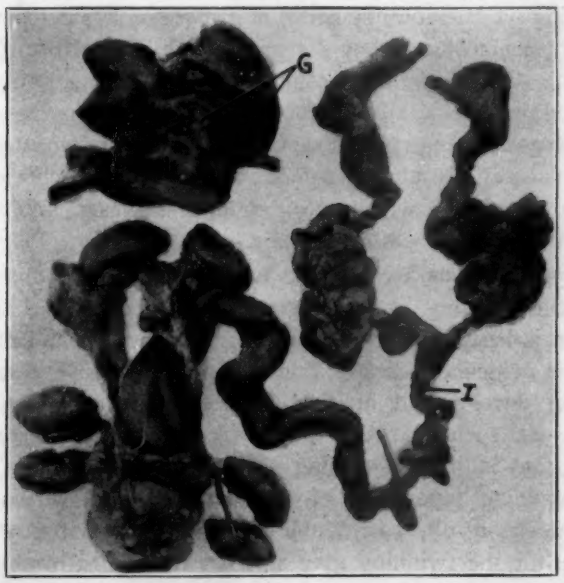

Fig. 5.—Photograph showing fused livers (*L*) with two gallbladders (*G*), fused intestines (*I*) with a common appendix and colon and pronounced dilatation of the rectum (*R*). The duodenum of baby 1 is dilated (*D*).

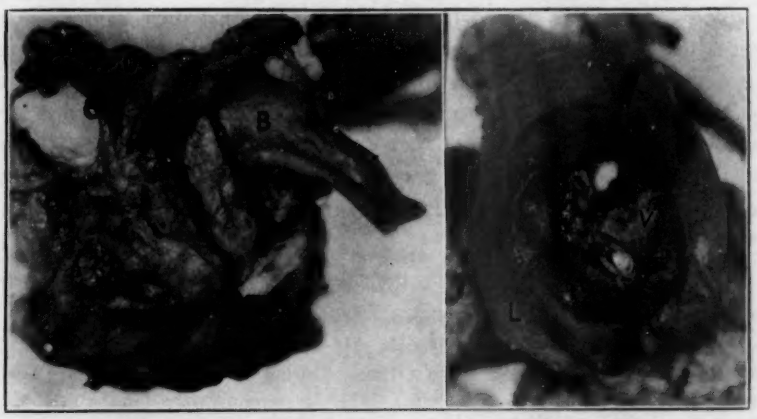

Fig. 6.—Photograph showing bicornuate uterus (*U*), urinary bladder (*B*) and common labia (*L*) and vaginal orifices (*V*).

Each uterus was partially bicornuate and contained a cervix. The fallopian tubes and ovaries were present and normal (fig. 6).

The central nervous system was not examined.

COMMENT

In the vast majority of cases the single fertilized ovum gives rise to a single individual enclosed in a single chorion. Occasionally, however, the ovum forms a single chorion enclosing within it a product of conception which shows evidence of a more or less complete progression toward the formation of 2 separate individuals from the original single ovum. Thus there may result parasitic monsters, double monsters or conjoined twins and at the end of the scale 2 quite separate individuals, true monozygotic twins. All, however, have two fundamental characters in common: they are always surrounded by a single chorion, and the sex, in those cases in which recognition of sex is possible, is always the same in both members of the pair.

Monozygotic twins are believed to be due to environmental abnormalities of the young, morphologically sound ovum. This theoretic explanation is based on sound embryologic principles and experimental studies; the evidence indicates that the primary cause is a temporary stoppage of development at a critical stage.[2] If the environmental conditions are such that this phase of developmental quiescence is prolonged, that is, if the twinning process is postponed too long, there is an incomplete separation of the embryos and various types of double monsters result.[3] In double monsters the environmental factors responsible for the twinning may also act further to produce reversed asymmetry and minor degrees of mirror imaging. In conjoined twins there is an additional growth-depressing factor, namely, growth rivalry between the 2 individuals, and the component showing the reversed asymmetry is physiologically inferior and less well developed.[2]

Double monsters are so infrequent that the statistics on their occurrences are not particularly accurate. Mall [4] collated the statistics of a number of observers and on the basis of about 100,000 cases estimated that approximately 7 per cent of all pregnancies terminated in aborted pathologic ova and about 0.6 per cent in malformed fetuses at term. Of the latter only a small portion were conjoined twins. Puech [5] examined a series of 100,000 births and found 517 malformations of

2. Newman, H. H.: Multiple Human Births, New York, Doubleday, Doran & Company, Inc., 1940.

3. Stockard, C. R.: Developmental Rate and Structural Expression: An Experimental Study of Twins, Double Monsters and Single Deformities, and the Interaction Among Embryonic Organs During Their Origin and Development, Am. J. Anat. **28**:115-277 (Jan.) 1921. Newman.[2]

4. Mall, F. P.: A Study of the Causes Underlying the Origin of Human Monsters, J. Morphol. **19**:3-368 (Feb.) 1908.

5. Puech, cited by Scammon, R. E.: Fetal Malformations, in Abt. I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1925, vol. 6, chap. 164, pp. 654-682.

various sorts. Of these only 2 were double monsters. Adair [6] reported 2 double monsters in 25,000 deliveries at the Chicago Lying-in Hospital and Dispensary. Mudaliar [7] attended the delivery of 4 double monsters which took place in the years 1920 to 1928, during which period about 25,000 deliveries were conducted at the Giffard School of Obstetrics, Madras, India. Rydén [8] reported 2 thoracopagi in 40,000 births in Lund, Sweden, from 1900 to 1933. At the Cook County Hospital there were 3 thoracopagi from 1905 to the present, during which time there were approximately 85,000 deliveries. It is interesting to compare these figures with those for the frequency of monozygotic twins, which are also forms of embryonic duplication. Monozygotic twins form about 25 per cent of all twins,[2] the ratio of all twins to single births being 1 to 85.2.[9]

Thoracopagi are by far the most common of the double monsters, Hirst [10] citing the incidence from his study of literature as 56 in 145, or 38.6 per cent. Ysander [11] reported 47 thoracopagi out of 153 double monsters described in the literature from 1911 to 1922, and we have found 78 additional ones in 192 double monsters from 1922 to the time of writing, including the present report. In the human species, female monsters are between two and three times as frequent as males. Curiously, monozygotic male twins seem to occur more frequently than females, approximately 10 to 8.6.[5]

In almost every case of thoracopagic monstrosity one finds a complete heart, more or less severely deformed on account of its location in the center of the malformation. The circulatory system presents a greater number of variations than probably any other part of the body. As a matter of fact, one might not be able to find 2 specimens which, no matter how similar they may appear in their external appearance and thoracic structures, would show similar abnormalities in the heart. Ysander [11] and Vintemberger [12] have attempted to simplify the classifi-

6. Adair, F. L.: Fetal Malformations in Multiple Pregnancy, Am. J. Obst. & Gynec. **20**:539-552 (Oct.) 1930.

7. Mudaliar, A. L.: Double Monsters: A Study of Their Circulatory Systems and Some Other Anatomical Abnormalities, and the Complications in Labour, J. Obst. & Gynaec. Brit. Emp. **37**:753-768, 1930.

8. Rydén, Å.: Delivery of Thoracopagus, Zentralbl. f. Gynäk. **58**:972-975 (April 28) 1934.

9. Greulich, W. W.: The Incidence of Human Multiple Births, Am. Naturalist **64**:142-153, 1930.

10. Hirst, J. C.: Monsters, in Piersol, G. M., and Bortz, E. L.: Cyclopedia of Medicine, Surgery and Specialties, Philadelphia, F. A. Davis Company, 1939, vol. 10.

11. Ysander, F.: Studies on the Morphology and Morphogenesis of Human Thorocapagic Monsters, with Special Reference to the Malformation of the Heart, Upsala, Almqvist & Wiksells, 1924.

(Footnotes continued on next page)

cation of these complex hearts and have shown that there is every variety, from two separate hearts, each in its own pericardial sac, to complete fusion of both auricles and ventricles in a common pericardial sac.

The main obstetric feature in the consideration of double monsters is the effect on parturition. At present there is no way of preventing the formation of monsters or of rectifying the abnormalities after they have developed. Double monsters have never been diagnosed before labor, though the presence of twins has frequently been established in such cases. Not until dystocia develops in the second stage of labor has the presence of conjoined twins been discovered, usually by vaginal or intrauterine examination. The majority of gross fetal malformations rarely go to term, because such a pregnancy tends to abort spontaneously, presenting no special obstetric problem. On the other hand, the presence of a fully formed double monster creates at once an obstetric problem of major proportions, fraught with potential danger to the mother. When it is certain that a major malformation exists, the welfare of the fetus or fetuses should be disregarded and a method of delivery chosen which is safest for the mother. Embryotomy is frequently the only form of delivery possible.

SUMMARY

A case of a human double monster, thoracoabdominopagus tetrabrachius tripus, is presented, consisting of 2 female fetuses united from shoulder girdle to perineum. One pair of upper extremities had a fusion of the soft tissues; the lower extremities on the same side had a common femur, a common tibia, separate fibulas and a common great toe. The common thorax contained four pleural cavities, a fused thymus, a common pericardial sac and two complete four-chambered hearts, mirror images of each other. A fused diaphragm separated the thoracic structures from a single peritoneal cavity. There were a large fused liver and two gallbladders with separate bile duct systems. The gastrointestinal systems were separate to their fusion at the ileum, forming a single ileum, appendix, colon and rectum. The anus was imperforated. Each twin had a complete and grossly normal urinary system. Each uterus was partially bicornuate and contained a cervix. The fallopian tubes, ovaries and vaginas appeared grossly normal. The single umbilical cord, attached to a common placenta, contained six vessels, two umbilical veins and four arteries, normal in origin and distribution.

950 East Fifty-Ninth Street.

6060 South Drexel Avenue.

12. Vintemberger, P.: Recherches sur l'inversion splanchique et la conformation du coeur chez les monstres doubles monomphaliens, Arch. d'anat., d'histol. et d'embryol. **6**:403-468, 1926-1927.

SPONTANEOUS AND HEREDITARY THROMBOPENIC PURPURA IN A MOTHER AND TWO SONS

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It is the purpose of this paper to present evidence supporting the concept of congenital thrombopenia as demonstrated by the case of a woman who had a splenectomy for thrombopenic purpura at the age of 14 years. The patient was twice pregnant and had two deliveries. Both children were male, and both succumbed to thrombopenic purpura in the neonatal period. Although the proved cases of congenital thrombopenia are so few as to make one consider it a relatively rare condition, it is probably more common than has been supposed. We believe this is the first report of its occurrence in two children of the same mother and as a result of two consecutive pregnancies.

In 1925 Rushmore [1] reported on purpura as a complication of pregnancy. He collected 6 cases in which the fetus showed symptoms similar to those of the mother and added a case of his own. Since that time 7 additional cases have been reported in the literature.[2] The case reported by Greenwald and Sherman [2e] was one of congenital thrombopenic purpura which developed in a girl between the tenth and the

From the Department of Pediatrics and the Department of Medicine of The Brooklyn Hospital.

1. Rushmore, S.: Purpura Complicating Pregnancy, Am. J. Obst. & Gynec. **10**:553 (Oct.) 1925.

2. (*a*) Waltner, K.: A Case with Congenitally Manifested Symptoms of Purpura Hemorrhagica, Jahrb. f. Kinderh. **106**:307, 1924. (*b*) Liebling, P.: Purpura Hemorrhagica Complicating Pregnancy: Both Mother and Child Were Affected and Recovered, Am. J. Obst. & Gynec. **11**:847 (June) 1926. (*c*) Conti, F.: Purpura in Pregnancy: Fatal Episode with Fetal Manifestations, Rassegna internaz. di clin. e terap. **14**:450 (May 31) 1933. (*d*) Siegler, S. L.: Purpura Hemorrhagica Complicating Pregnancy, M. Rec. **139**:189 (Feb. 21) 1934. (*e*) Greenwald, H. M., and Sherman, I.: Congenital Essential Thrombocytopenia, Am. J. Dis. Child. **38**:1245 (Dec.) 1929. (*f*) Sanford, H. N.; Leslie, E. I., and Crane, M. M.: Congenital Thrombocytopenia, ibid. **51**:1114 (May) 1936. (*g*) Brown, D. N., and Elliott, R. H. E.: Results of Splenectomy in Thrombocytopenic Purpura: Comparative Study of Ten Cases in Which Splenectomy Was Performed and Eleven Cases Treated by Conservatvie Methods, J. A. M. A. **107**:1781 (Nov. 28) 1936. (*h*) Davidson, L. T.: Congenital Thrombopenia, Am. J. Dis. Child. **54**:1324 (Dec.) 1937.

fourteenth day of life and terminated in death. Their careful histologic studies and analysis of the blood established a definite diagnosis and brought out several points worthy of mention. Studies of the bone marrow showed a deficiency in the number and quality of the megakaryocytes. They observed poor development of these cells and absence of specific granulations in the cytoplasm. This supports the theory advanced by Frank [3] that the disease "depends on a lack of megakaryocytes or an inadequate function of these cells, as visualized by the absence of granules." It is also noteworthy that the case reported by Greenwald and Sherman presented other congenital abnormalities in addition to the deficiency of the bone marrow.

Sanford, Leslie and Crane [2f] reviewed the literature on congenital thrombopenia and added a case. In their case, studies of the blood were made of a mother and her infant after a pronounced reduction of platelets was noted in both patients. There was a history of a similar purpuric rash in the maternal grandmother. The infant girl made an uneventful recovery and was discharged from the hospital on the tenth day of life without evidences of hemorrhage, despite a consistently low platelet count. No mention was made of studies of bone marrow in this report. The authors explained the absence of severe or fatal hemorrhages on the basis of increased disintegrative ability of the platelets, which kept the coagulation mechanism in balance.

Brown and Elliott [2g] mentioned a case of congenital thrombopenia in their report on the results of splenectomy for this disease. A more detailed study of the same case was later published by Davidson.[2h] The mother, known to have thrombopenic purpura, was delivered of a full term baby girl who showed classic signs of the disease. This case is in many respects similar to our own. However, in their case the infant was female and the outcome favorable. In our case both infants were male and the outcome unfavorable. Apparently the most helpful of the various therapeutic measures tried was the injection of bothrops antitoxin. This was not used in our case.

REPORT OF CASES

CASE 1.—In 1926, E. W. F., then 14 years of age, was admitted to the Hartford Hospital with the diagnosis of thrombopenic purpura. Laboratory examinations showed a low platelet count and an increased bleeding time. A splenectomy was done, and bleeding tendencies were immediately controlled. After this procedure the patient remained well, except for an occasional purpuric spot. In July 1938, when she was 26 years of age, she became pregnant. The antepartum period was entirely uneventful. No bleeding tendencies were encountered. Laboratory studies during that period showed a negative Wassermann reaction. There

3. Frank, cited by Greenwald and Sherman.[2e]

were 70,000 platelets present. The bleeding and clotting times, red blood cell count, hemoglobin content and white blood cell count were within normal limits.

On March 6, 1939 the patient was admitted to The Brooklyn Hospital while in active labor. Labor totaled sixteen hours, and the patient was delivered of a 6 pound 4½ ounce (2,849 Gm.) living boy. The delivery was uneventful and was terminated by a low forceps control. Nitrous oxide, oxygen and ether anesthesia was used. The postpartum course was uneventful. There were no bleeding tendencies. The platelet count was 70,000. There was no retraction of the clot at the end of forty-eight hours. Bleeding and coagulation times on repeated determinations were one and three minutes. The Rumpel-Leede phenomenon was not elicited. The patient was discharged from the hospital on March 20, 1939 with no clinical evidence of the disease.

The patient again became pregnant in January 1940. Laboratory studies done in April showed 62,000 platelets present. There was no retraction of the clot in thirty-three hours. The prothrombin time, estimated by a modification of the Quick method, was 28 per cent faster than normal. During the antepartum period the patient was kept under careful supervision and received large doses of vitamins A, D and E and elements of the B complex, as well as calcium. During the last three months of pregnancy 1 mg. of synthetic vitamin K (menadione) was administered daily by mouth, and liver extracts parenterally.

The second pregnancy terminated about one month prior to the expected date, culminating in the delivery of a 5 pound 5½ ounce (2,424 Gm.) boy. The labor and delivery were entirely normal except that there was rather profuse bleeding from the episiotomy wound and vaginal tears. As in the first pregnancy, the postpartum course was uneventful. Results of studies of the blood made at this time were essentially the same as those of the tests made in April, previously mentioned. About six months after delivery a sternal aspiration was performed.[3a] The total count showed 86,800 cells per cubic millimeter (all the nucleated cells); there were 67 megakaryocytes per cubic millimeter. A survey of the megakaryocytes disclosed the cytoplasm to be finely granular throughout and vacuolated at the periphery. Platelet formation, which is usually observed recurring from the edges of the cell, was entirely missing. The structure of the platelets in the blood smear corresponded to the fine granulation of the cytoplasm.

At the time of writing this patient is clinically well, except for the occasional appearance of purpuric spots.

CASE 2.—At birth this boy was well developed, weighed 6 pounds 4½ ounces (2,849 Gm.) and measured 18½ inches (47 cm.) in length. Many purpuric spots, varying from the size of a pinpoint to an area 0.5 cm. in diameter, were noted over the entire body. Physical examination revealed no other abnormalities. The baby was given 20 cc. of paternal blood intramuscularly (immediately). There was no bleeding from the cord or other sign of active hemorrhage for the following two days. The platelet count taken on the first day was 80,000; the bleeding time was one minute and the clotting time three and one-half minutes. The clot retraction time was not determined. On the third day the baby showed signs of intracranial hemorrhage and died within twenty-four hours.

Necropsy.—The outstanding observation at necropsy was evidence of widespread and fairly extensive bleeding, both in the skin and in the internal organs. The skin over the entire body was marked with small purpuric hemorrhages,

3a. Studies of the bone marrow were made by Dr. Carl Smith of New York Hospital.

varying in diameter from 1 or 2 mm. to 1 cm. These were innumerable over the face, scalp and extremities and somewhat less numerous on the trunk. Similar small hemorrhages were noted in the mucous membranes of the eyes, nose and mouth (fig. 1).

The subcutaneous tissues of the scalp contained a small amount of hemorrhagic fluid. The cranium appeared tenser than normal with rather marked separation of the fontanels and suture lines. When the cranial cavity was opened, about 50 cc. of fluid blood was found overlying the left cerebral hemisphere in the subdural space. Most of this had been released when the skull was opened. Above and below the tentorium an additional 100 cc. of firmly clotted blood was

Fig. 1 (case 2).—Baby A, showing purpuric hemorrhages over the entire body, most pronounced on the extremities, face and scalp.

found. This appeared to have arisen in a tear of the left leaflet of the tentorium, the blood lying both among its torn fibers and around it. There was no hemorrhage into the subarachnoid space and no evidence of hemorrhage into the brain tissue.

The pleural, pericardial and peritoneal cavities contained no excessive fluid and no blood, but scattered petechial hemorrhages were noted over both the visceral and parietal layers of the pleura and pericardium. Further evidence of the hemorrhagic diathesis was found in the mucous membranes of numerous structures. Mucosal hemorrhages were noted in the esophagus, larynx, trachea, larger bronchi, stomach, small intestine and bladder. The amount in each was insufficient to disturb the general contours of these organs, which were otherwise grossly normal. Their lumens were full of blood.

The heart was of normal appearance, showing no anomalous developments; the ductus arteriosis was patent, and the foramen ovale was not completely closed. The lungs were well aerated and on section showed no extensive hemorrhages.

The thymus was of normal appearance except for petechial hemorrhages beneath its capsule. It weighed 9 Gm.

The spleen, which weighed 11 Gm., was firm and purplish red; hence the malpighian corpuscles did not stand out distinctly.

The liver showed no gross abnormalities and weighed 117 Gm.

The kidneys seemed slightly larger than normal, but their gross configurations were not altered. Each weighed 19 Gm. The adrenal glands presented no unusual features.

None of the superficial or deep lymph glands were enlarged.

Microscopic Examination.—The sections substantiated the gross observations and revealed little else of note. There was moderate congestion of all viscera and small mucosal hemorrhages in several of them, as grossly noted. All organs were well preserved except the liver, which showed a moderate amount of fatty infiltration of its parenchyma. Hemopoietic foci were scattered widely throughout this organ. The bone marrow of the vertebral bodies and ribs showed nothing of note. Immature leukocytes and red blood cells were present in normal amounts. The bone marrow slides were also studied by Dr. N. Rosenthal, of New York,[4] who expressed the opinion that megakaryocytes were present and normal. The peripheral blood picture appeared normal in all respects.

Anatomic Diagnoses.—The diagnoses were: term delivery; neonatal death; congenital thrombopenic purpura; intracranial hemorrhage; acute passive congestion of the viscera.

CASE 3.—This baby, the 5 pound 5½ ounce boy previously mentioned, cried spontaneously and vigorously immediately after delivery. The skin was apparently clear at birth, but with removal of vernix a few minutes after delivery petechial spots were seen in both groins and around both ankle joints. The remainder of the physical examination made at this time showed nothing unusual. There was no bleeding from the cord or mucous membranes. The liver and spleen were not palpable. Laboratory examinations made during the first hour after birth gave these results: There were 90,000 platelets present; a differential white cell count showed 21 per cent polymorphonuclear leukocytes, 60 per cent lymphocytes, 4 per cent endotheliocytes and 4 per cent eosinophils; only 3 myelocytes and 6 erythroblasts were seen in 200 white cells counted. The bleeding time was eleven minutes; the clotting time, one and one-half minutes. The prothrombin time was 28 per cent of normal.

During the first hour after delivery the patient was given a transfusion of 55 cc. of whole blood into the vein from a professional donor. Synthetic vitamin K (menadione) (1 mg.), ascorbic acid (100 mg.) and koagamen (a hemostatic preparation from shepherd's purse) (2 cc.) were administered intravenously. This therapy was followed with one tablet of menadione by mouth the evening of the day of birth. Despite treatment the hemorrhagic spots continued to appear on the surface of the skin until the following morning, when they were so numerous as to become confluent and there were large areas of ecchymoses over the dependent portions of the body. At this time hemorrhagic areas appeared on the lips and mucous membrane of the mouth.

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4. Rosenthal, N.: Personal communication to the authors.

Laboratory studies were repeated about eighteen hours after birth. The hemoglobin content was 100 per cent, the red blood cell count 5,550,000 and the white blood cell count 12,900, with polymorphonuclear leukocytes 47 per cent, lymphocytes 46 per cent, endotheliocytes 3 per cent, eosinophils 3 per cent and basophils 1 per cent. A smear showed polychromatophilia, normoblasts, decreased platelets and disintegrating forms of polymorphonuclear leukocytes. The platelet count at that time was 130,000, the bleeding time one minute and the clotting time two minutes. The prothrombin time was 42 per cent of normal.

The clinical picture became rapidly worse during the second day, and periods of cyanosis and apnea were noted. The cry became high pitched and feeble, and there was a suggestion of bulging of the fontanel. Despite a second transfusion

Fig. 2 (case 3).—Baby B, showing pronounced cyanosis and confluent hemorrhagic areas over the entire body.

of whole blood, oxygen therapy and general supportive measures, the baby died almost exactly twenty-four hours after birth.

Necropsy.—The body was that of a fairly well nourished white boy, weighing 5 pounds 5 ounces (2,396 Gm.) showing rather extreme cyanosis of the skin and mucous membranes. In addition, the skin contained innumerable large and confluent hemorrhagic areas covering practically the entire surface of the body (fig. 2). The mucous membranes of the mouth showed similar hemorrhagic areas, and the entire buccal mucous membrane appeared reddish. There was slight fulness of the anterior fontanel, but no definite tension was noted. No other abnormalities were found on external examination.

When the skull was opened, a considerable amount of blood was encountered beneath the periosteum. The cranial bones appeared normal. Numerous small punctate hemorrhages were seen on the dural lining, but no gross accumulations

of blood were found in the cranial cavity. The tentorium cerebelli and the falx cerebri were intact and showed no evidence of laceration. The brain proper presented a normal configuration and intimal structure.

Except for evidence of hemorrhages the viscera and serous surfaces showed relatively few changes. The pleural cavities contained 1 to 2 cc. of bright red blood in each sac, and the visceral pleura showed focal and diffuse hemorrhages throughout (fig. 3). The lungs appeared dark red as a result of multiple small hemorrhages. The pericardial and peritoneal cavities and membranes were free of frank blood. The peritoneal cavity contained a slight excess of amber-colored fluid. Mucosal hemorrhages were noted in the esophagus and stomach. Larger

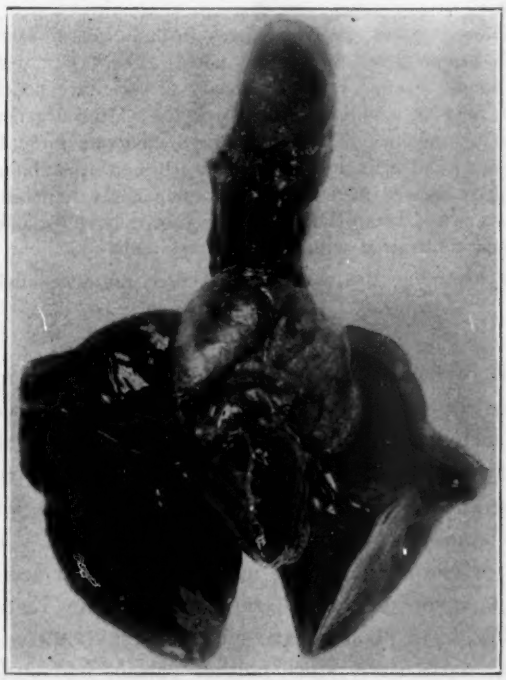

Fig. 3 (case 3).—Heart, lungs and thymus gland of baby B, showing extensive hemorrhages into the lungs. Hemorrhagic areas are noted on the thymus and pericardium, the latter being diffuse and confluent.

and diffuse hemorrhagic areas were found involving a large portion of the wall of the small intestine along the countermesenteric surface of the loops. These hemorrhages became more conspicuous and of a deeper red color near the ileocecal valve and were prominent on the peritoneal coat of the appendix, giving the latter a generally purplish red, mottled appearance. Scattered focal petechial hemorrhages were widely distributed throughout the mesentery. Small punctate hemorrhagic foci, accounting for a more or less confluent hemorrhagic appearance, were found underlying the capsule of the liver. The parenchyma, however, showed no evidence of hemorrhages.

The spleen, although of normal size, was of firmer consistency than normal and presented a deep purplish red appearance. Several enlarged lymph glands from the mesentery similarly appeared dark red.

The heart was of normal size and appearance, presenting no structural abnormalities. The foramen ovale was functionally closed, and the ductus arteriosus was patent and of normal size.

The kidneys did not appear unusual. The adrenal glands and the thymus appeared grossly normal.

Microscopic Examination.—The bone marrow showed an apparently normal development save for sparsity of megakaryocytes. This was confirmed by Dr. Rosenthal,[4] who stated that the few megakaryocytes which were seen were immature in type.

All viscera showed rather similar changes, with advanced passive congestion and parenchymal hemorrhages as grossly noted. The latter were particularly abundant in the lungs. Many of the pulmonary alveoli were poorly aerated and contained edema fluid in addition to erythrocytes. Mild degenerative changes were seen in the myocardium. The liver showed moderate fatty degeneration of its cells. Scattered foci of cells undergoing active hemopoiesis appeared in no way unusual. The spleen showed moderate polymorphonuclear infiltration in addition to passive congestion and hemorrhages. The enlarged lymph glands showed congestion, edema and infiltration with inflammatory cells.

Anatomic Diagnosis.—In this case, the diagnosis was congenital thrombopenic purpura.

COMMENT

A diagnosis of hemorrhagic disease of the newborn in these cases was not tenable for various reasons. The spontaneous and immediate appearance of hemorrhagic phenomena in both infants following birth was not characteristic of hypoprothrombinemia. The findings from prothrombin studies made on the second baby were within normal limits and not unusual for infants in this age group. The adequate administration of vitamin K to the mother during her second period of gestation and intravenous administration of vitamin K to the second infant soon after birth should have eliminated hypothrombinemia, had it been present, particularly since neither patient had suffered damage to the liver. The less intensive studies of the blood of the first infant and the more exhaustive studies made for the second baby showed an unmistakable deficiency of platelets. It is also significant that neither infant responded to the administration of whole blood.

The disease present in these cases, moreover, did not fit into the familial hemorrhagic group first described by Glanzmann.[5] This hereditary hemorrhagic thromboasthenic syndrome is characterized by a normal number of platelets. These platelets demonstrate morphologic changes and a failure to produce normal clot retraction.

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4. Rosenthal, N.: Personal communication to the authors.

5. Glanzmann, E.: Hereditäre hämorrhägische Thrombasthenie. Ein Beitrag zur Pathologie der Blutplättchen, Jahrb. f. Kinderh. **88**:1 and 113, 1918.

Interesting to contemplate is the treatment for infants so afflicted. Obviously the therapy in our cases was inadequate. One conjectures whether immediate splenectomy or irradiation of the spleen might be of value. The use of snake venom has been approved by some observers but found useless by others.

The advisability of pregnancy in a patient with essential thrombopenic purpura must be considered. The patient here reported has been advised against further childbearing.

Dr. J. Arnold deVeer made the pathologic studies in these cases.

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Progress in Pediatrics

ANCIENT PROCESSES IN A SCIENTIFIC AGE

FEEDING ASPECTS

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Many of the difficulties encountered in caring for young children are, as a matter of fact, due to the disarrangement caused by the impact of new technics on the child's ancient mechanism. The disturbances are of the same order as those which might be expected if one tried to install a supercharged motor on a model T chassis. Streamlined modern methods may not necessarily work out successfully when applied to a baby of stone age vintage.

For at birth the 1942 edition of the human infant is the oldest thing in the world! Each newborn child is actually a living replica of the individual that came into the light of day long before the dawn of history. This seeming anachronism occurs because evolutionary changes take place very slowly as compared with the lightning-fast modifications caused by civilized life. To understand human nature, one must recognize how thin and superficial is man's veneer of culture, at best a mere gloss over the surface which cracks and breaks at the slightest strain. Such reversions to barbarous behavior are even called babyish, because they are primitive and so are babies.

Under average conditions, however, children born with this primeval equipment gradually come to take on the sort of personality and behavior approved of in the modern world. Keeping in mind the extremely deep and wide gap between primitive life and modern urban existence, it is easy to understand why the civilizing process should be difficult and why it should take considerable time for its development. But, particularly in the last few years, this civilizing effort has been concentrated in an attempt to cram the adjustment into the first few years of life. That is one reason why so much difficulty has been encountered in child care during this period.

In this so-called training process the child is under the compulsion of two major forces, each of which is highly dynamic. The first and more primitive is made up of the growth drives of the baby. This force is undoubtedly the most exacting restraint that is ever imposed on any one. To grow, not only in the physical but in an emotional and mental sense, according to one's own preordained pattern is hard discipline; but

this is the sort of discipline which every person must endure during his first few years of life if he is to attain any personal competence at all.

The other compelling influence is the impact of the customs of society. This force will often dictate to the young baby such intimate and personal matters as when and how much to eat, when and how much to sleep and when to eliminate, as well as when and how to conform to the more complicated technics included in civilized behavior.

It is not ordinarily understood how compelling the latter force has become, particularly when it is backed up by medical instructions. The reason is easy to see. Almost within the memory of the present day physicians, medical science has grown from an art which was almost like witchcraft to a science which has reduced the dangers of living in the modern environment to a surprising degree. Because physicians can point with pride to the fact that under optimal conditions and under their control the child mortality rate has been cut to a point where almost no well-born infants die, their advice has become heavily weighted with authority. Unfortunately their advice on training, as far as the care of small children is concerned, has been unbelievably concentrated in the direction of rigid routines, with the result that these rigid routines have been backed by the full authority of the profession. One finds, then, the babies squirming on the horns of a dilemma: on the one hand, driven by their own native developmental trends, and on the other, restricted by the authoritative routines of a scientific age. The effect of this situation has been to set up inevitable conflicts, which will be illustrated later. The point to remember at the outset is that it is not the baby's fault. He did not ask to be born with his own particular propensities, nor did he ask to have these technics inflicted on him.

The obvious solution of such a problem in lack of synchrony is to make adjustments somewhere along the line. Up to the present time it has been very difficult to make cultural adjustments, because it is characteristic of adults to feel that when their children are concerned "mother is always right." The result has been that the babies have been expected to make all of the adjustments. I submit that they have done a very creditable job. In fact, when it is thoughtfully considered, this remarkable ability of human babies to adjust to a difficult environment is the factor which has made civilized living possible, if indeed one may claim "civilized living" in 1942.

I shall approach this discussion of the difficulties encountered in feeding babies with the idea that the child is neither good nor bad but just *is*—as he was made by his heredity. It is not fair to pass judgment on his acts without considering all of the evidence. Pediatricians, as his friends and advisors, should be the first to realize the situation. Apparently nobody else does.

To get down to fundamentals, then, why is it that a baby often refuses to nurse, even when his mother's breasts swell with milk? Why is it that

he is likely to refuse cereal, no matter in what sort of china it is served? Why does he pick, dally and fuss over his food and make adults concede ridiculously, in spite of the fact that the urge to eat is fundamental? Let us investigate the interplay of the two great forces just described as they affect a child's ability to become a competent eater and see what can be "civilized living" in 1942.

At the time he is born, the normal child is equipped with several adequate reflexes, or behavior patterns, which are designed to make him a successful feeder from the breast. The most obvious of these reflexes are those concerned with the actual getting of food—rooting, sucking, swallowing and satiety reflexes.

The rooting reflex is the first one of these to come into play. When a baby smells milk, he moves his head around and attempts to find its source. If one cheek is touched by a smooth object, he will turn his mouth toward that object and open it in anticipation of grasping the nipple. This obviously gives a clue as to how milk should be given to the baby. His cheek applied to his mother's breast will start him rooting with his mouth for the nipple.

I can illustrate a mistake made in this regard by telling the recent experience of a patient in one of our best hospitals. As I was making daily rounds, she said to me: "Your nurses don't know their stuff!" In answer to my surprised inquiry as to what she meant, she said: "They don't know anything about the rooting reflex. They bring my baby in, place her beside me and with their hand on the baby's cheek try to push her head around to meet the nipple. The baby, feeling the pressure of the hand, tries to turn toward the nurse's palm instead of toward my breast. A fight ensues, and usually the natural response is prevented. I always tell the girls to go out of the room; that I can handle this myself if they will just lay the baby down beside me. I touch her cheek with my breast and let her do the rest." This experienced mother had learned to respect her baby's ability in these basic matters. This is a highly important lesson for anybody to learn.

The sucking reflex, of course, is called out as soon as the baby grasps the nipple. This enables him to draw milk into the back part of the throat, whence it is routed down to the stomach by the highly complicated swallowing mechanism. This involves the safe transport of milk past the opening to the lungs and down the gullet into the stomach. This ability is next only to the ability to breathe in safeguarding a child's life, because if milk is aspirated into the lungs a very dangerous condition may result, leading to pneumonia and sometimes to death.

The importance of this fact is most evident in taking care of premature or weak babies. In many 7 month babies the swallowing reflex is not yet completely developed, so that when milk finds its way into the

back of the throat it is as likely to go down the windpipe as down the gullet. Fortunately there is a way to tell whether or not a baby is able to swallow, because the sucking reflex matures at the same time as the swallowing reflex and any baby who sucks vigorously will swallow. The obvious lesson to learn from this fact is that no baby too immature to suck should ever be expected to swallow. The only safe way to feed such a child is by means of a stomach tube. Any of the various gadgets, like the Breck feeder, which force milk into the baby's mouth before he is able to suck are extremely dangerous, even in the most experienced hands, and in my opinion should never be used.

The other factor in his nursing equipment which makes him efficient as a feeder is his ability to know whether or not he has had enough. One might call this the satiety mechanism. Many people might even challenge the existence of such a mechanism, since its workings are entirely unknown, but it must be obvious to any one familiar with the growth and development of babies that unless such an accomplishment had grown up throughout the evolutionary period the race could never have survived. Something must have told prehistoric babies when to go and when to stop in eating.

Closely allied to the latter ability is the hunger-appetite sequence, which exerts itself to tell a child not only when to stop and go in his meals but how to select the foods he eats.

The mechanism of the hunger phase of this sequence is well recognized and understood, because hunger can be physiologically demonstrated. The sensation called hunger is caused by vigorous contractions of the wall of the stomach which occur rhythmically throughout the day. That these vigorous contractions actually cause pain has been demonstrated several times experimentally by means of a rubber balloon which the baby can swallow into his stomach. When partially inflated, this balloon can be made to register gastric movements on a drum, demonstrating their synchrony with his hunger cries. This sensation of hunger is probably the first unpleasant feeling that most babies get after they are born and placed in their warm cribs. One of the attributes of hunger is that the instant any form of nutriment touches the gastric wall the cramps immediately cease.

In this faculty can be seen the beginnings of the second phase of the sequence, appetite, because the relief from pain which results from swallowing gives the baby a pleasant response to food. This relief is experienced over and over again for days, weeks and months. Thus every baby comes to associate comfort with eating, and as he learns that different sorts of foods give him the same familiar comfort, the whole eating process becomes enjoyable to him. It is believed that appetite really is a much more complex function of the body than just this

pleasurable or comfortable response, because recent evidence has made it clear that through his appetite a child is able to select and choose the amounts and kinds of food which are needed for his growth. Here again it is impossible to explain the exact way that this comes about. The important thing to recognize is the presence of this intricate ability, whether or not one understands how it works.

All of these things just mentioned are born into each baby as part of his inherent ability. To them are added, however, many other factors which are brought about by his growth. One of the most important and interesting of these is closely related to the appetite ability just discussed; that is the child's capacity to increase or decrease his intake according to his needs. During his first few months the baby gradually increases the amount of milk he takes from the bottle and later he does the same for food from the spoon and cup. Still later, between the second and fourth years of life, most children find it natural to reduce the number of calories they ingest, and one finds the typical run-about child eating from one half to two thirds as much food as is taken by his year old brother. Obviously it is the reduced speed of his growth which calls for this rather radical reduction in the amount of food taken. Again, during the preadolescent period, without any outside instruction, children gradually increase their appetite until they reach the rapid spurt of growth at adolescence and consume unbelievable amounts of food in this process. Finally, from this period on there is a gradual falling off of appetite until again in old age a very small amount is found necessary.

Still more concrete abilities of babies add to their eating efficiency. One of these is the reflex which makes it possible for a child to carry food from the front of his mouth to the back of his throat. When solid food or a spoon is applied to the lips of a newly born baby, it is invariably thrust out by his protecting tongue, which makes it next to impossible to feed him in this manner. The only way a newly born baby can get food by this method is by being placed on his back with the mouth held open so that gravity carries the nourishment into his pharynx. After that, the swallowing reflex takes control, and food goes into his stomach. Between the ages of 3 and 4 months, however, practically all babies make a decided change in their mouth behavior. When food approaches the lips, they open and the tongue actively takes the nourishment back, so that swallowing is easy. This obviously marks the time when children are equipped to take thick foods.

A little later, soon after the six month period, whether or not teeth have erupted, one finds babies making chewing motions with their jaws. This activity gives us a clue to the time when lumpy or solid particles may be given, because only after this time can they be masticated into suitable size for swallowing.

While these changes have been going on, a neuromuscular coordination of the arms and hands has been developing, so that the baby first grasps and holds his bottle with the hands, next learns to hold a cup and finally learns to manipulate such sophisticated eating implements as the spoon, fork and knife. The changes in methods of feeding which go with this growth of muscular ability also indicate the time at which babies can take over more and more of their own feeding. At 4 or 5 months they begin to be able to hold their own bottles; from 6 to 9 months they can do something in the way of feeding themselves with a cup; and by 18 months they can do a fair job of self feeding with a spoon. After these abilities have been consummated, adult attendance is unnecessary at meals. In fact, most children do much better if they are left to their own devices.

I have just outlined the ancient forces in the baby which enable him to become a successful feeder. How does this all work out under the heavy hand of modern technic? How does the hunger-appetitite mechanism fare today in the average hospital? It is evident to any one that the baby's rhythmic hunger pains are completely ignored in his schedule for feeding. The newly born baby who wakes up with a stomach-ache and announces his epigastric crisis by shrieking cries does not meet the response nature intended for him. Instead of being picked up and given something to eat, he is made to wait until hands of the clock on the wall move around to the approved hour of the day, at which time, sleeping or screaming, he is picked up and fed. This rigidity of management, no matter how helpful it may be for the smooth running of the hospital, definitely blocks the baby's eating ability in two or three ways. In the first place, unless he is under the influence of hunger pains, his first few feedings will not give him the grateful relief from distress which he was intended to experience. In the second place, when a sleeping baby is awakened to nurse at the breast by some of the methods commonly used in hospitals, spanking, dashing with cold water or snapping his feet and hands, he acquires an unpleasant, rather than a pleasant, response to the whole eating complex. Eating is not the eager delight it should be, and the next meal is likely to meet with a more antagonistic response from him. This inconsiderate handling of the first few meals of life is the only adequate cause I know for so-called anorexia nervosa congenita. I have never seen such lack of appetite in a newly born baby who was allowed to eat when he began to cry with hunger pains.

Another common factor which interferes with a young baby's eating is the increasing use of sedatives given to the mother before delivery. Most of the barbiturates, while they are undoubtedly beneficial in relieving distress in the mothers, do give rise to a certain amount of stupor in the babies. This artificial languor which is so evident in

these babies seems to dull their early responses so that they do not care to eat, sometimes for as long as three or four days. If this factor is recognized and the babies are allowed to become thoroughly awake before attempting to nurse, their feeding abilities emerge in due time.

Another way in which the scientific methods interefere with a baby's early feeding is in the rigid application of rules about the length of time he may nurse or about the amount of food put into his supplementary bottles. If a child has taken his fill at the breast, no amount of pushing or hauling will be successful in making him take more food. All that happens is that the forcing disgusts him with the whole unpleasant process. It is just as important, on the other hand, to allow him to nurse as long as he desires, so that he will come away from his feeding completely satisfied. This is as true with bottle feeding as it is with breast feeding. For fifteen years I have never restricted any baby in the amount of food he took from breast or bottle, and I have never seen a newly born baby who would overeat when so handled. Unless his satiety mechanism is allowed to mature he cannot become a successful feeder.

Under the regimen practiced in most hospitals, babies are denied the satisfaction of the 2 a. m. feeding, in spite of the fact that practically all babies awaken in the early morning hours and demand with shrieks and wails to have their stomachs filled. The argument in favor of this restriction is that the babies will sleep through the night if they are broken of this habit. As a matter of fact, I have never seen a baby who would awaken for a 2 a. m. feeding after he was 6 weeks old if the feedings were offered him whenever he cried at night. It is a part of their growth and development that they eliminate this early morning feeding before that time. In the interest of satisfactory meals and the comfort of babies during their early days, is seems reasonable to allow them this nourishment until their own development marks the time for its discontinuance. The same observation holds for the 10 p. m. feeding, which is given up voluntarily by babies after they are a few months old. The proper time for the elimination of these night feedings is when babies stop asking for them.

To the casual observer, what has just been said about allowing babies freedom of choice in their meal times may seem to advocate an irregular regimen for children, and this would be quite true were it not for the fact that the average baby is at least as regular as the kitchen clock. In his own body resides the rhythmic mechanism which awakens him for meals at approximately the same moment day in and day out. Each baby has his own individual time interval, which remains approximately the same over long periods and can be safely relied on to indicate his nursing needs. However, as a practical point, the baby's own demands need not be too rigidly adhered to after the first two or three days of life, because he is a very accommodating sort of

person. After the first few meals are given to him and he becomes accustomed to the relief from pain which follows, he will usually be glad to eat at any time the food is offered to him. This is why most babies can be adjusted to a four hour regimen. The ones that cannot be held over to this schedule are usually happy on a three hour routine.

As the baby grows older and acquires new abilities to eat, as just outlined, the careful physician will see to it that when he shows the ability and desire to hold his bottle, manipulate the cup and feed himself with a spoon he is given the opportunity to learn these new technics. If he is denied the opportunity when he first shows the desire, because it makes for messy feedings, he may become fixed in baby ways of eating and may not respond with more mature behavior when the family thinks he should. Similarly, it is futile to attempt spoon feeding until the baby's tongue activity shows that he has reached this point of maturation. If an attempt is made earlier to force semisolids down his throat, he is likely to be frightened or irritated and to obstruct, rather than to help, his feeding program.

When the baby's jaws begin to chew is the obvious time to introduce lumpy sorts of food. If this is done, the baby takes the food naturally and becomes a good "chewer." On the other hand, if the cue is missed, he is likely again to be fixed at an infantile level and to continue to demand sieved foods long after the time his own inclinations would lead him to masticate.

The increase and decrease in the appetite urge of children is often ignored completely, and this ignoring of the normal decrease which occurs in run-about children results in undue urging of food and is one of the commonest causes for the anorexia prevalent in such children. If every mother could realize that her 3 or 4 year old child should eat about two thirds as much as he did when he was a year old, one would not see so much forcing of food at this age.

Another development trait, which occurs in relation to nap time at about 1 year of age, leads to a great deal of confusion as to the proper time to introduce the baby to a three meal schedule. At this age it is customary to feed children at 7 and 10 in the morning and 2 and 6 in the afternoon. The baby at this same time does a peculiar thing in connection with his sleep habits: He gives up his afternoon nap and clings to his late morning nap, when one would expect him to be "raring to go" after his all night sleep. Most infants enjoy the 10 o'clock bottle before this late morning nap. Suddenly, however, they give up this life-long habit and decide to stay awake all morning and to sleep after their lunch. If a mother observes her child carefully, she will never miss this obvious shift, and this is the moment at which she will begin to feed him on a strictly three meal schedule, with breakfast from 7 to 8, dinner from 11 to 12 and supper from 5 to 6.

While none of these factors which I have just discussed is of great immediate importance to the welfare of the baby, the sum total may indicate the degree of competency which he develops as an eater. When it is remembered that this substantial list of difficulties has to do only with the feeding of the baby and that the same sort of influences are active in establishing his competency in sleeping, eliminating and other habits, it is easy to understand why the study of normal growth and development is important in the routine management of children. It is the physician's duty to introduce the child to his habits in the world in such a way that he can accept them as natural and right. To control these factors which are so tremendously important in future life is a great opportunity which physicians today should be glad to accept.

707 Fullerton Avenue.

News and Comment

PERSONAL NEWS

Dr. Howard B. Mettel Appointed.—National headquarters of the American Red Cross has announced the appointment of Howard B. Mettel, M.D., as director of medical and health service of the midwestern area, American Red Cross, with headquarters in St. Louis.

Dr. Mettel comes to the Red Cross from the Indiana State Health Department where he has served as director of the maternal and child health program and as director of the crippled children's program of Indiana. He also was associated with the teaching staff of the Indiana University School of Medicine.

GENERAL NEWS

Rachford Memorial Lectures.—Dr. Hattie E. Alexander, of Columbia University, will deliver the eleventh annual series of lectures under the auspices of the Benjamin Knox Rachford Lectureships, in Cincinnati on Thursday, Nov. 12, and on Friday, Nov. 13, 1942, at 8:15 p. m., in the auditorium of the Children's Hospital Clinic and Research Building. The subjects of her lectures will be "Experimental Basis for Treatment of Haemophilus Influenzae Infections" and "Treatment of Haemophilus Influenzae Infections and of Pneumococcic and Meningococcic Meningitis."

The American Board of Pediatrics.—The dates for the spring examinations of the American Board of Pediatrics have been determined, as follows: March 27 and 28, 1943, in St. Louis, and April 24 and 25, in New York. The written examinations for those taking the spring examinations will be held locally, under a monitor, on February 12.

Those who wish to take the oral examination in March 1943 must have been registered for it before Dec. 1, 1942, and those taking the examination in April must have been registered before Jan. 1, 1943.

CORRECTIONS

In the article by Drs. Earl W. Flosdorf and Aims C. McGuinness entitled "Studies with Haemophilus Pertussis: VIII. The Antigenic Structure of Haemophilus Pertussis and Its Clinical Significance," in the July issue (Am. J. Dis. Child. **64**:43, 1942), footnote 9 should include a reference to the report by Drs. Bradford and Slavin, the second article cited in footnote 6.

In the last line of the first paragraph of the article by Drs. Bronstein, Luhan and Mavrelis entitled "Sexual Precocity Associated with Hyperplastic Abnormality of the Tuber Cinereum," in the August issue (Am. J. Dis. Child. **64**:211, 1942), "and particularly without involvement of the hypothalamus" should read "particularly lesions of the hypothalamus."

Abstracts from Current Literature

Biochemistry; Bacteriology, and Pathology

BACTERICIDAL EFFECT OF ULTRAVIOLET RADIATION. HARVEY C. RENTSCHLER, RUDOLPH NAGY and GALINA MOUROMSEFF, J. Bact. **41**:745 (June) 1941.

The authors describe a simple method for uniformly seeding the surfaces of Petri plates with bacteria, making it possible to obtain a quantitative study of the action of ultraviolet radiation under varied conditions. An integrating ultraviolet meter which responds only to the bactericidal wave band was devised, which would eliminate errors of exposure due to fluctuations in the intensity of the light and in the character of the emitted radiation. The variation in the resistivity of the individual bacteria in a culture to ultraviolet radiation was shown to be considerably greater than was heretofore suspected; this explains many discrepancies generally attributed to other causes. In a normal culture of bacteria of a species such as Escherichia coli the resistance of different bacteria at the same stage of the life cycle to ultraviolet rays was not the same, and the same individual organism was shown to have a widely different resistance to ultraviolet radiation at different stages of its life cycle. The temperature of an organism at the time of irradiation had a negligible influence on the lethal action of the ultraviolet radiation provided the temperature did not cause injury. The average resistance to ultraviolet radiation of the individual cells of different types of bacteria is considered by the authors to be roughly of the same order of magnitude, and they believe that the apparent large variation was due to clumping and shielding.

STOESSER, Minneapolis.

STUDIES ON MICROORGANISMS IN SIMULATED ROOM ENVIRONMENTS: I. A STUDY OF THE PERFORMANCE OF [illegible]E WELLS AIR CENTRIFUGE AND OF THE SETTLING RATES OF BACTERIA THROUGH THE AIR. EARLE B. PHELPS and LEON BUCHBINDER, J. Bact. **42**:321 (Sept.) 1941.

In this paper, which is the first one of the series, the authors show that when a broth culture of bacteria is sprayed into the air of an experimental chamber a certain fraction of the nuclei resulting from evaporation of the spray droplets and containing viable bacteria have measurable settling velocities. Under their experimental technic, settling proceeds at such a rate that about 20 per cent of those bacteria-laden particles capable of settling do so during each hour and this geometric rate of decrease results in a residual population in the air at the end of twenty-four hours of about 0.5 per cent of the initial number capable of settling. The communication is technical and should be examined for details.

STOESSER, Minneapolis.

STUDIES ON MICROORGANISMS IN SIMULATED ROOM ENVIRONMENTS: II. THE SURVIVAL RATES OF SEREPTOCOCCI IN THE DARK. LEON BUCHBINDER and EARLE B. PHELPS, J. Bact. **42**:345 (Sept.) 1941.

This is the second paper based on the experiments which were undertaken to determine the survival rates of that portion of bacteria which settle to the floor. The methods used by the authors were designed to simulate conditions obtaining when bacteria are sneezed or coughed into air by a person. They found that in a dark room the estimated time for 50 per cent survival for the three strains of streptococci studied namely, group A and group B beta hemolytic and alpha hemolytic, varied from about one to thirteen days.

STOESSER, Minneapolis.

STUDIES ON MICROORGANISMS IN SIMULATED ROOM ENVIRONMENTS: III. THE SURVIVAL RATES OF STREPTOCOCCI IN THE PRESENCE OF NATURAL, DAYLIGHT AND SUNLIGHT, AND ARTIFICIAL ILLUMINATION. LEON BUCHBINDER, MATHILDE SOLOWEY and EARLE B. PHELPS, J. Bact. **42**:353 (Sept.) 1941.

In the third paper of this series the authors describe a method which measures the lethal effect of light—daylight and sunlight through a window and artificial light—on bacteria in a simulated room environment. Bacteria were allowed to settle out of a fine spray of broth in air on filter paper in Petri dishes and the covers were replaced; the plates were then exposed to light, poured with agar and incubated. It was found that daylight on clear or cloudy days is a potent lethal agent for streptococci. While it has been known for a long time that daylight passing through glass in the absence of sunlight is bactericidal, the qualitative and quantitative analysis of the effect and comparison with the corresponding effect of sunlight in simulated room environments as well as its possible relation to the public health has not been seriously considered. The authors' studies indicate that daylight and direct sunlight probably play an important role in the suppression of streptococcic and other infections of the upper respiratory tract. They noted that an average of about fifty minutes' exposure to daylight is necessary to destroy 50 per cent of the organisms of a strain of alpha hemolytic streptococci. A strain of beta hemolytic streptococcus of Group B was somewhat less susceptible, while a strain of beta hemolytic streptococci of group A was distinctly less susceptible than either of these.

STOESSER, Minneapolis.

CULTURES OF THE DYSENTERY GROUP ISOLATED IN WESTERN MICHIGAN. MARY BRANSTON and GRACE ELDERING, J. Infect. Dis. **68**:113 (March-April) 1941.

One hundred and twenty-three cultures of dysentery bacilli isolated in western Michigan have been studied as to their cultural and serologic reactions. The Sonne type of dysentery culture predominated during the period covered by the study. Fifty-six Sonne cultures were isolated, as compared with 24 cultures of the Flexner group. In addition, there were isolated 31 cultures of Bacillus alkalescens and 12 incompletely identified cultures of dysentery bacilli.

TOOMEY, Cleveland [AUTHORS' SUMMARY].

GROWTH FACTORS FOR HEMOPHILUS INFLUENZAE AND HEMOPHILUS PARAINFLUENZAE. A. BASS, SAM BERKMAN, FELIX SAUNDERS and STEWART A. KOSER, J. Infect. Dis. **68**:175 (March-April) 1941.

Cysteine did not replace hemin as a growth factor for four strains of Haemophilus influenzae. Preparations of crystalline beef liver catalase and highly purified horse liver catalase replaced hemin as the "X" factor. The catalase preparations also were capable of replacing the coenzymes for growth of Haemophilus, thus apparently supplying a substance functioning as the "V" factor.

Study of comparative heat stabilities of catalase and of coenzymes I and II did not support the assumption that the growth-promoting activity of catalase was due to the presence of coenzyme as impurity. Other possible explanations are presented and discussed.

In addition to coenzyme I (or coenzyme II) and hemin, the influenza bacilli appear to require one or more other factors. This factor cannot be replaced by pantothenic acid, cocarboxylase, riboflavin, ascorbic acid, vitamin B_6 and inositol; the further addition of catalase was likewise of no value in promoting growth. Some sources of this unknown factor are indicated.

TOOMEY, Cleveland [AUTHORS' SUMMARY].

Metabolism; Infant Feeding; Milk and Other Foods

THE CHANGES IN THE BLOOD PRODUCED BY DEHYDRATION IN INFANCY. A. G. V. ALDRIDGE, Arch. Dis. Childhood **16**:81 (June) 1941.

The changes in the blood in a series of 51 infants showing varying degrees of dehydration (35 suffering from gastroenteritis and 16 from pyloric stenosis) have been studied.

The red blood cell count was raised, the average count being well over 5,000,000 per cubic millimeter, and it has been shown that this represents a considerable increase in the red cell count in infants of this age, although some of the increase may be due to nutritional anemia. The hemoglobin content was also increased, but often to a less degree than the red cell count because of the presence of hypochromic anemia. Estimation of the hemoglobin content alone was not an adequate indication of hemoconcentration. When allowance was made for age and any nutritional anemia that may have been present, the hematocrit reading was considerably above normal.

The plasma chloride in gastroenteritis was variable, the average for the series was raised (651 mg. per hundred cubic centimeters) but in some cases the values were below normal. The height of the plasma chloride did not necessarily vary with the degree of dehydration or clinical condition. It was shown that an apparent, if not actual, rise in concentration of plasma chloride in gastroenteritis and dehydration is due to (1) the relatively small amount of chloride as compared with base lost; (2) the concentration of the circulating blood, and (3) renal insufficiency. In pyloric stenosis the plasma chloride was either diminished slightly or near the lower limit of normal.

The plasma protein level in infants with gastroenteritis was on the average a little higher than in a series of normal infants. The plasma protein concentration cannot be used as an indication of the state of hydration of the circulating blood. In pyloric stenosis it was slightly above normal. In this series of cases no definite relation was found between concentration of plasma protein and blood cell count, hemoglobin content and hematrocrit reading, except that all values tend to be raised above normal in dehydration. KELLY, Milwaukee.

THE CALCULATION AND PRESCRIBING OF INFANTS' FEEDS. I. AFTER THE NEONATAL PERIOD: THE USE OF STANDARD MIXTURES. II. THE NEONATAL PERIOD: PRACTICAL POINTS IN THE REGULATION OF FEEDS IN MATERNITY HOSITALS AND HOMES. HELEN M. M. MACKAY, Brit. M. J. **1**:841 (June 7); 888 (June 14) 1941.

In these articles the author describes the difficulty occurring when evacuated children are taken to some reception center and medical care of the feeding is being adjusted. In the articles "the routine feeding of newborn babies is discussed, and a formula is suggested whereby their approximate daily calorie needs can be calculated." The employment of feeds providing 20 calories per fluidounce (30 cc.) for all infants, unless there is some special contraindication, is strongly urged on the ground that thereby (*a*) there is a much reduced risk of quantitative mistakes for the infant, (*b*) feeding is greatly simplified for doctors and nurses, and (*c*) labor is lessened in children's wards or day nurseries.

Tables are given for the instruction of nurses in infant feeding. These can be adapted and shortened by the doctor in accordance with the type of feeding he habitually uses. It was hoped that feeding, standardized to the extent here suggested, may be widely adopted at the present time, for it offers a way of coping with the difficulty of ordering feeds for large numbers of babies brought into reception areas on feeds of every description. ROYSTER, University, Va.

THE MANAGEMENT OF BREAST FEEDING. S. L. LUDBROOK, New Zealand M. J. **40**:95 (April) 1941.

The author discusses the physiology of lactation and the details of breast feeding, including position, interval, duration and weight records. Causes of

failure of breast feeding (faults of management and faults on the part of the mother), the mother's diet, care of the breasts, insufficiency of secretion, vomiting, diarrhea and constipation as seen in the newborn are also given consideration.

WEIGAND, Indianapolis.

Vitamins; Avitaminoses

DARK ADAPTATION AND VITAMIN A: FURTHER STUDIES WITH THE BIOPHOTOMETER. P. C. JEANS, EVELYN L. BLANCHARD and FRANKLIN E. SATTERTHWAITE, J. Pediat. **18**:170 (Feb.) 1941.

Observations on dark adaptation as determined by means of the biophotometer are reported. Evidence is presented that the results obtained with this instrument are consistent from test to test of the same subjects and correspond with the vitamin A status of those subjects when the technic employed is satisfactory and when certain interpretations are applied. Normal subjects with ample vitamin A intake while in good health have normal results at all times. The subjects of this observation group who had poor dark adaptation and who submitted to therapy attained normal adaptation in all instances while receiving vitamin A. In the geographic region in which these observations were made dietary deficiency alone seemed to be the cause of impaired dark adaptation in few instances. The most frequent and usual cause of impaired adaptation seemed to be a utilization deficiency resulting from illness, especially illness resulting from infection. A seasonal incidence of dysadaptation was observed, corresponding to periods in which the greatest number of infections occurred. In the case of an orphanage in which the children were received approximately 2,000 U. S. P. units of vitamin A in the diet daily, no instances of abnormal dark adaptation were observed during a winter period of observation. In a group of 120 school children 5 per cent had dark adaptation not wholly normal in the fall. In the winter almost 20 per cent had abnormal adaptation. In the spring only 1 child of 50 tested had an abnormal result, and this child gave a borderline result.

RAUH, Cincinnati [AUTHORS' SUMMARY].

VITAMIN P AND CAPILLARY FRAGILITY. HOWARD G. RAPAPORT and SYLVIA KLEIN, J. Pediat. **18**:321 (March) 1941.

Capillary fragility in a group of 100 allergic children was studied by means of a positive pressure test. Forty-nine per cent had abnormal capillary fragility. In a subsequent, more detailed study, 12 children with repeated abnormal reactions to capillary fragility tests were given vitamin P (calcium eriodictate) and followed periodically for at least six months. In all of the 12 children the results of the capillary fragility tests became normal after the administration of vitamin P.

Vitamin P apparently plays an important role in the mechanism of permeability of the capillary wall, probably acting as an essential constituent for normal capillary permeability.

RAUH, Cincinnati [AUTHORS' CONCLUSIONS].

Hygiene; Growth and Nutrition; Public Health

SOME SEX DIFFERENCES OBSERVED IN A GROUP OF NURSERY SCHOOL CHILDREN. JEANETTE B. MCCAY and MARIE B. FOWLER, Child Development **12**:75 (June) 1941.

In a study of the health and development of 31 girls and 35 boys enrolled in the junior nursery school of the New York State College of Home Economics at Cornell University during the five years 1932 to 1937, some interesting sex differences were noted. Although these differences were too small to be statistically significant in themselves, their direction is of interest as giving further

evidence in line with the results of others' studies. An increasing number of reports in the fields of biology, psychology, physiology and even nutrition points toward constitutional variations between the sexes, and the reports present a rather consistent view.

In general, the males of this group were distinguished from the females by taller, heavier bodies, by more food eaten at dinner, particularly the foods of high caloric value like breadstuffs and desserts, and by more restless movements during the noon meal. The boys of the group tended to awaken earlier in the morning than the girls, which shortened their night's sleep and lowered the total amount of sleep gained during the twenty-four hours.

THE BERKELEY GROWTH STUDY. HAROLD E. JONES AND NANCY BAYLEY, Child Development **12**:167 (June) 1941.

Sixty-one children born in Berkeley, Calif., in 1928 and 1929, have been tested and measured repeatedly at the Institute of Child Welfare of the University of California. "The problems investigated have dealt chiefly with motor, mental and physical development, observed from birth and with the plan of continuing to maturity." This report presents the general program of the study. The sample is described, and the tests, measures and procedures are outlined. A bibliography of thirty-five titles lists all publications which have been based on this research to date.

SERUM PHOSPHATASE IN INFANTILE SCURVY. HARRY SHWACHMAN, J. Pediat. **19**:38 (July) 1941.

Serum phosphatase studies were carried out on 18 patients with scurvy. The average phosphatase value of the serum of these patients on admission to the hospital was 3.2 Bodansky units, with a range of 1.1 to 4.9 units, as compared with the mean value for normal infants of approximately 7.2, with a range of 4.5 to 12 units. A substantial rise in serum phosphatase occurs within approximately one week after the institution of vitamin C therapy. Evidence from the literature suggests that bone is the major source of serum phosphatase and that this enzyme may serve as an index of osteoblastic activity. Increased serum phosphatase in active rickets is consistent with the overactivity of the osteoblastic tissue found in this disease. In scurvy the pathologic picture is one of inactivity or inability of the osteoblasts to form bone matrix. The low level of serum phosphatase reflects this state of affairs. Administration of vitamin C in scurvy institutes morphologic changes in the osteoblastic tissue indicative of recovery in a very short time. This healing is reflected in a rise of the serum phosphatase level, which was observed in these patients within one week.

RAUH, Cincinnati.

LESIONS OF THE OPTIC NERVE IN VITAMIN B_1 DEFICIENCY. T. K. RAMAN and C. ABBU, J. Indian M. A. **10**:417 (July) 1941.

This study was concerned with 15 cases of beriberi, 10 cases of pellagra, 4 cases of avitaminosis B_1 (peripheral neuritis without cardiovascular disturbance and edema), 2 cases of toxic peripheral neuritis (peripheral neuritis and tachycardia without edema), 1 case of beriberi combined with pellagra and 2 cases of diabetes mellitus. Definite concentric contraction of the field of vision was found in 5 patients with beriberi, 2 with avitaminosis B_1, 4 with pellagra, 1 with beriberi and pellagra and 1 case of diabetes mellitus; slight concentric contraction was found in 3 patients with beriberi and 2 with pellagra. Primary atrophy of the optic nerve was seen in 1 patient with pellagra and in 1 with avitaminosis B_1. There seemed to be no correlation between the symptoms of peripheral neuritis and the lesion of the optic nerve. Improvement in the fields of vision occurred after treatment with a liberal diet and vitamin B_1 in 3 patients with beriberi and 2 with pellagra and associated vitamin B_1 deficiency. GONCE, Madison, Wis.

Newborn

ANTEPARTUM USE OF VITAMIN K IN THE PREVENTION OF PROTHROMBIN DEFICIENCY IN THE NEWBORN. GEORGE P. BOHLENDER, WILLIAM M. ROSENBAUM and EARL C. SAGE, J. A. M. A. **116**:1763 (April 1) 1941.

Fifty mothers were given a vitamin K preparation (4-amino-2-methyl-1-naphthol hydrochloride) intravenously during labor. Fifty others served as controls. A marked reduction in prothrombin time occurred in all cases, even when the administration occurred five minutes before delivery. Because of the easy and consistent transfer through the placenta the authors advocate that this preventive of hemorrhage in the newborn infant be given to all mothers.

The same preparation can be given intravenously to infants manifesting hemorrhage.

Observations in control cases agreed with those reported by other authors.

HEERSMA, Kalamazoo, Mich.

HEMORRHAGIC DISEASE OF THE NEWBORN: A REPORT OF THREE HUNDRED AND FIFTY-EIGHT CASES. LENDON SNEDEKER, J. Pediat. **19**:1 (July) 1941.

Snedeker presents an analysis of the cases of hemorrhagic disease of the newborn occurring at the Boston Lying-in Hospital from 1874 to 1937 and from the Infants' Hospital from 1914 to 1937. This analysis was made to evaluate the results secured by treatment with transfusion. The patients whose cases are here presented were observed during the period before and after transfusion therapy was introduced. Experience with these cases showed that the mortality in hemorrhagic disease may be reduced from 57 per cent without transfusion to less than 20 per cent if transfusion is used. Data from these cases suggest that hemorrhagic disease is not a specific disease but a clinical syndrome, unrelated to congenital syphilis, infection or erythroblastosis foetalis. Trauma and asphyxia seem to be etiologic factors of importance. Prothrombin deficiency appears to be the cause of at least one form of hemorrhagic disease. More data are needed on the prothrombin levels in normal and bleeding infants and on the effect of maternal diet, transfusion and vitamin K on these levels.

RAUH, Cincinnati.

MENINGITIS IN A NEWBORN DUE TO THE COLON BACILLUS. P. A. MCLENDON and R. H. MITCHELL, South. M. J. **34**:1001 (Sept.) 1941.

McLendon and Mitchell report the recovery of a 3 week old infant with meningitis due to Bacillus coli communis.

The newer chemotherapy promises to lower the mortality of B. coli meningitis. Meningitis due to the colon bacillus is rare, but this is the predominating organism causing the disease in the newborn period.

The author believes that an early diagnosis of meningitis in newborn infants is difficult owing to the lack of signs and symptoms. SCHLUTZ, Chicago.

TREATMENT OF HAEMORRHAGIC DISEASE OF THE NEWBORN. A. I. S. MACPHERSON, Brit. M. J. **2**:433 (Sept. 27) 1941.

In this article the author first gives a brief review of the development of the treatment of hemorrhagic disease of the newborn and states that profound hypoprothrombinemia is now recognized as a characteristic abnormality of the blood in this condition and that any method of treatment can be measured by its capacity (1) to raise the prothrombin content of the plasma so rapidly that the hemorrhage stops in a short time and (2) to maintain the prothrombin at so nearly normal level that the hemorrhagic tendency does not recur. The article discusses 10 cases in which true hemorrhagic disease of the newborn has been treated by injection of whole blood in the buttocks, by a blood transfusion or by the

injection of vitamin K analogues. In the cases in which treatment was by injection of whole blood intramuscularly the change in the prothrombin time was so slight and so transient that the treatment was of no avail. In the 2 cases in which blood transfusions were used there were rapid improvement in the prothrombin index and early cessation of bleeding. In both, however, subsequent bleeding showed an almost equally rapid fall of the prothrombin index. In 3 cases in which vitamin K analogues given after hemotherapy had failed to control the hemorrhage or to raise and maintain the prothrombin index there was an immediate and lasting response both from the clinical standpoint and in the level of the prothrombin index. In each instance frank bleeding stopped in a short time and the prothrombin index rose to and remained at a normal or nearly normal level. In addition to these cases, the author reports 2 cases of icterus gravis in which the patients showed spontaneous hemorrhages and were treated successfully with vitamin K analogues. From a therapeutic point of view the interesting feature was the rapid and sustained effect given by a vitamin K analogue, even when a levulose tolerance test indicated a considerable depression of hepatic function.

In his discussion the author points out that repeated transfusions of large amounts of blood are not without danger and that the great majority of transfusions must be administered in a hospital. He recommends, because of the simplicity of the administration of vitamin K and the extreme rarity of conditions in which vitamin K analogues will not be effective in arresting hemorrhagic disease, that one of these analogues be employed in all cases of spontaneous and persistent bleeding in the newborn. He adds, however, that in most cases in which prolonged or massive hemorrhage is exsanguinating the patient, simultaneous treatment by transfusion and injection of a vitamin K analogue should be given.

ROYSTER, University, Va.

HEPATIC HEMORRHAGE IN STILLBORN AND NEWBORN INFANTS: A CLINICAL AND PATHOLOGICAL STUDY OF FORTY-SEVEN CASES. J. L. HENDERSON, J. Obst. & Gynaec. Brit. Emp. **48**:377 (June) 1941.

Hepatic hemorrhage is reported in 47 of a series of records of 1,312 autopsies collected by the writer from the two principal maternity hospitals in Edinburgh. Holmberg and Adair, in studies of just over 1,000 and of 1,046 autopsies, report an incidence of hepatic hemorrhage in approximately 5.6 per cent and 5 per cent, respectively. In the author's series of cases, rupture of the liver with intraperitoneal hemorrhage was found in 24 cases, an unruptured subcapsular hematoma in 22, and a deep-seated laceration in 1. It has been conclusively demonstrated that complicated labor is the cause of hepatic hemorrhage in the fetus during birth. External trauma is the principal precipitating factor, but asphyxiation is an important cause. Multiparity, with its greater attendant risks, seems to be an important factor. In this series, 26 mothers were over 30 years of age and 13 were over 35. There were 33 multiparas. Fetal position was abnormal in half of the cases. The author does not discuss in detail the mechanism of the traumatic element.

Hemorrhage occurs most frequently on the anterior surface of the right lobe of the liver, which is the most exposed part of the organ. The author believes that the sacral promontory and the symphysis of the mother are the principal traumatizing agents. The higher incidence in breech deliveries is probably accounted for by the greater amount of manipulation of the trunk which is necessary in such cases. The majority of hepatic hemorrhages are produced during birth, but the condition may occur antenatally and postnatally. In the former type, fetal manipulations, such as external version, trauma to the abdomen by falling and eclamptic fits, have been incriminated. In the postnatal type, violent methods of resuscitation were regarded by earlier authors as one of the chief causes of damage to the infant's liver. In only 3 cases of the series was the delivery of the mother normal and spontaneous.

The bleeding usually arises from a superficial contusion or laceration of the parenchyma of the liver, and the capsule is not torn by the original trauma in the majority of cases. Thus a hematoma is formed varying in size from a small blood blister to a large accumulation of blood covering an extensive area of the surface of the liver. The hematoma may burst at any time with massive intraperitoneal hemorrhage. When the original trauma is severe enough to tear the capsule, the bleeding is more profuse, and the child is usually stillborn. Intracranial hemorrhage was also found in 20 of these patients. Signs of asphyxia were found in three fourths of the patients. Hemorrhages in various other locations were seen in 16 of the patients. One of the stillborn infants had a fractured femur and another a fractured clavicle.

The incidence of hepatic hemorrhage was three times as great in stillborn infants as in those who were born alive. Only 1 of the infants with fatal hemorrhage lived longer than a week. The incidence is much higher in abnormally large infants and in premature infants than in those weighing 5½ to 8 pounds (2,895 to 3,630 Gm.).

Hepatic hemorrhage in the newborn may be suspected in infants showing a sudden onset of signs of severe illness, the most outstanding and characteristic of which is the sudden appearance of severe anemia (in 19 of 37 infants born alive). Dyspnea, restlessness and crying, signs of shock and abdominal distention are not infrequently seen. Cyanosis and vomiting are other signs mentioned. Paracentesis may confirm a diagnosis of intraperitoneal hemorrhage from ruptured subcapsular hematoma or from any other origin. Laparotomy with suture of the rent in the capsule of the liver was successfully performed in 1 case mentioned by the author.

ADAIR and FREUNDLICH, Chicago.

DERMATITIS HERPETIFORMIS DUHRING IN A NEWBORN INFANT. H. WILLI and W. BURCKHARDT, Kinderärztl. Praxis **12**:144 (May) 1941.

This is a description with photographs of a case of dermatitis herpetiformis in a newborn infant weighing 3,380 Gm. The diagnosis was established by the characteristic rash as well as by the following findings: (1) The content of the vesicles was sterile; (2) in this fluid and also in the blood an extreme eosinophilia (up to 46 per cent) was found; (3) a patch test with 10 per cent potassium iodate in petrolatum led to the production of a herpetiform lesion on the skin. The disease lasted for over six months. The baby gained weight, however, and progressed normally in spite of the extensive cutaneous lesions. Treatment of the skin consisted of potassium permanganate baths and applications of 1 per cent silver nitrate and of powder.

HEYMANN, Cleveland.

Acute Contagious Diseases

OLFACTORY MUCOSA AS A POSSIBLE SOURCE OF ANTIPOLIOMYELITIC SUBSTANCES. ROVELLE H. ALLEN and PAUL F. CLARK, J. Infect. Dis. **68**:53 (Jan.-Feb.) 1941.

The soluble components of olfactory mucosa of a naturally resistant animal (the calf) failed to neutralize the poliomyelitis virus consistently. One of the acid-precipitable proteins (fraction B) in three different series protected some of the animals, but this protein was effective only when the quantity of virus used did not greatly exceed the minimal infective dose.

Since the olfactory membranes of the living susceptible animal are probably never subjected to very large amounts of virus at any one time, it seemed advisable in these neutralization tests to administer quantities approaching in size the minimal infective dose. The results, however, were often very irregular and demonstrated that such an approach is not suitable. There were indications that certain of the protein fractions possess weakly neutralizing properties, which

might have been demonstrated further by inoculation of large series of animals and a statistical consideration of the results. But the necessity of using the costly monkey as an experimental animal prohibited such studies. When the proteins were mixed with relatively large amounts of the virus they invariably failed to inhibit the development of the disease.

The antipoliomyelitic substance demonstrated in the nasal washings of certain persons by Amoss and Taylor has certain properties in common with lysozyme: they are both water soluble and thermolabile and appear to be diminished in certain stages of inflammatory conditions of the upper respiratory tract. Yet with one exception, lysozyme prepared from two different sources (egg white and human saliva) proved in our hands to be ineffective. Manifestly, these in vitro studies may not adequately approach the conditions found in the living animal.

TOOMEY, Cleveland [AUTHORS' DISCUSSION].

FAILURE OF TREATMENT OF EXPERIMENTAL POLIOMYELITIS WITH POTASSIUM CHLORATE. SIDNEY O. LEVINSON and ALBERT MILZER, J. Infect. Dis. **68**: 171 (March-April) 1941.

Potassium chlorate has no therapeutic value in experimental poliomyelitis.

After this paper went to press Gsell (*Schweiz. med. Wchnschr.* **70**:803, 1940) reported that he treated 97 of 119 patients with poliomyelitis during an epidemic in 1939 with Contat's method of administration of fractionated doses of potassium chlorate and noted that the medication failed to influence the course of the preparalytic stage of the disease, to prevent paralysis and to arrest severe forms of the disease with ascending paralysis.

TOOMEY, Cleveland [AUTHORS' CONCLUSIONS].

THREE STRAINS OF POLIOMYELITIS VIRUS ISOLATED FROM FECES DURING THE 1939 BUFFALO AND DETROIT EPIDEMICS. J. EMERSON KEMPF and MALCOLM H. SOULE, J. Infect. Dis. **68**:188 (March-April) 1941.

Three strains of the virus of poliomyelitis were isolated from eighteen samples of feces from 18 patients with typical clinical infections. The specimens were obtained at various times during the four weeks following the onset of paralysis. The strains were passed serially through monkeys, their identity thus being established. There were no significant differences in the degree of paralysis produced by the three strains, nor was there a significant change in the degree of paralysis after several passages of the viruses. The success or failure of primary isolation of the virus from feces and its establishment in monkeys seemed to depend in part, at least, on individual differences in the susceptibility of the monkeys.

TOOMEY, Cleveland [AUTHORS' SUMMARY].

A REPORT OF CLINICAL EXPERIENCE WITH MENINGOCOCCUS MENINGITIS. JOHN H. MCLEOD, J. Pediat. **18**:210 (Feb.) 1941.

The author reports on a series of patients with meningococcic meningitis treated over a five year period. Meningococcus antitoxin, antimeningococcus serum and sulfanilamide were used. McLeod concludes from the results obtained that:

1. All cases of meningococcic meningitis should be serologically grouped as soon as the diagnosis is made.

2. Antitoxin and sulfanilamide should be administered immediately until the results of grouping are known.

3. Should there be no clinical improvement after a reasonable length of time, a serum with the highest protective action in mice against the group found should be administered and sulfanilamide therapy continued. RAUH, Cincinnati.

Acute Infectious Diseases

STUDIES ON THE VIRUS OF PSITTACOSIS CULTIVATED IN VITRO. H. Y. YANAMURA and K. F. MEYER, J. Infect. Dis. **68**:1 (Jan.-Feb.) 1941.

The virus of psittacosis has been successfully cultivated in the fluid medium of Li and Rivers and the solid agar medium of Zinsser, FitzPatrick and Wei and propagated in the yolk sac of the developing chick embryo.

American, South American, Mexican and Australian strains of the virus have been grown with equal ease.

The "Maine" strain, isolated from an American parrakeet, has been maintained by cultivation for two and one-half years through 252 serial passages without loss of virulence.

Virus multiplication is intimately associated with tissue survival.

In the fluid medium the factors of utmost importance to virus multiplication are living susceptible tissues, certain physiologically essential salts and an optimal tissue-fluid ratio.

Under optimal conditions virus growth is a function of the incubation period and of the concentration of the inoculum.

The virus of psittacosis has been observed multiplying in mesenchymal cells, fibroblasts, epidermal epithelium, liver cells and macrophages of chick embryo tissues without any peculiar affinity for certain types of cells.

The fluid culture medium has been used as a means of titrating a virus suspension; but the practicability of this method is limited by a strictly aseptic technic. It is as sensitive as the mouse.

The microscopically discernible developmental stages of the psittacosis virus in cultures correspond with those reported by previous investigators. The name Mircrobacterium multiforme psittacosis has priority rights over the designation of L. C. L. bodies for the elementary bodies etiologically responsible for psittacosis.

Virus cultures, especially on the solid agar medium, are excellent sources of material for the production of vaccines and antigens.

TOOMEY, Cleveland [AUTHORS' SUMMARY].

A CYTOPHAGIC REACTION EMPLOYED IN THE DIAGNOSIS OF BRUCELLA INFECTION. MOGENS JERSILD, J. Infect. Dis. **68**:16 (Jan.-Feb.) 1941.

A description is given of a cytophagic test for brucellosis using patients' inactivated serum, bacterial suspension and citrated blood without opsonins.

This test shows that serum from patients with undulant fever contains immune opsonins at an early phase of the disease.

The reaction is more sensitive than agglutination and complement fixation. It has certain advantages over the cytophagic reaction of Huddleson, as the blood does not need to be examined soon after collection; besides, it reveals an inhibition of the phagocytosis which occurs when there is an especially high opsonin content in the blood. After a cutaneous test (with Huddleson's brucellergen) there occur immune opsonins, most markedly if there is already a small amount of antibody in the blood. If the cutaneous reaction is positive there occurs an abundance of antibodies (agglutinins, complement-fixing bodies and immune opsonins), an expression of the fact that a previously infected organism can quickly mobilize its antibodies. TOOMEY, Cleveland [AUTHORS' SUMMARY].

LABORATORY INFECTIONS DUE TO BRUCELLA. K. F. MEYER and B. EDDIE, J. Infect. Dis. **68**:24 (Jan.-Feb.) 1941.

The handling of cultures or specimens or the inhalation of dust containing Brucella organisms is eminently dangerous to laboratory workers. A review of the published records of such professional infections is amplified by an analysis of 74 cases of brucellosis observed among bacteriologists, pathologists and other

workers who in the course of their duties were exposed to Brucella in the laboratories of the United States. The nature of their disease was proved by blood cultures and by serologic tests. All three types of Brucella were involved in these infections, which caused in about half the patients an illness of from one to two weeks and in the other half a prolonged and serious malady extending over months. The protective measures are discussed, and evidence is presented to indicate that antigen injections with dead vaccines fail to prevent laboratory infections.

TOOMEY, Cleveland [AUTHORS' SUMMARY].

INFLUENZA VIRUS STUDIES DURING THE 1939 EPIDEMIC IN CENTRAL EUROPE. R. M. TAYLOR and MIKLÓS DREGUSS, J. Infect. Dis. **68**:79 (Jan.-Feb.) 1941.

During an epidemic of influenza which occurred in central and eastern Europe in January 1939, 16 virus strains were isolated from points as far removed as Warsaw, Poland, and Szeged, on the southern border of Hungary.

The serologic studies so far completed indicate that these strains form a group which differs considerably from PR8 (American) and W.S. (English). They are more closely related to the CHR and TAL English strains.

Specimens of material from the throats of 21 persons were examined for virus, and the acute and convalescent serums were tested for the neutralizing antibody titer. Fourteen of the 21 persons showed a rise of titer in the convalescent serum, and from 11 (78 per cent) of these a virus was obtained. No virus was obtained from any of those who failed to show a rise in the titer following the attack.

Of the initially inoculated ferrets which subsequently were shown to be infected with virus, 40 per cent gave no significant febrile response. All except 1 of the strains were rather easily adapted to mice after one or more ferret passages, but from only 2 of 12 specimens containing the virus was it possible to transmit the infection directly to mice.

Differences in the specificity of the immune response in human beings and ferrets are discussed.

TOOMEY, Cleveland [AUTHORS' SUMMARY].

CERTAIN BROAD EPIDEMIOLOGICAL ASPECTS OF INFLUENZA. R. M. TAYLOR; ALADAR PETRILLA and MIKLÓS DREGUSS, J. Infect. Dis. **68**:90 (Jan.-Feb.) 1941.

An analysis of the morbidity declarations during the last decade of complicated influenza in Hungary reveals that at least two different forms of disease are included under this diagnosis. One is bunched in epidemic proportions and affects more or less evenly all age groups; the other occurs with seasonal sporadicity and is confined largely to the age group below 10 years. Laboratory investigations extending over the last four years indicate that the former disease is caused by influenza A virus, while the latter is not. The implications of these observations are discussed.

A review of evidence suggests that influenza A tends to involve wide geographic areas during the same years and is therefore pandemic rather than epidemic in its extent.

TOOMEY, Cleveland [AUTHORS' SUMMARY].

THE PRIMARY ISOLATION OF SMALL COLONY STRAINS OF EBERTHELLA TYPHOSA FROM BLOOD, FECES, URINE AND SPUTUM. JANIE F. MORRIS, T. F. SELLERS and A. WILSON BROWN, J. Infect. Dis. **68**:117 (March-April) 1941.

From a total of 10 cases of typhoid fever, small colony strains of Eberthella typhosa were isolated 6 times from blood, 9 times from feces, 4 times from urine and twice from sputum.

An effect similar to the satellite phenomenon of Grassberger as related to Haemophilus influenzae is described. Certain peculiarities of cell morphology

were observed. From one blood strain, a substrain was obtained which was composed chiefly of aberrant cells; long, fusiform filaments and branching and budding forms were seen. This pleomorphic characteristic has remained constant for two years.

The size of the colonies depended on the medium employed. The colonies averaged about 0.2 to 0.3 mm. in diameter on infusion agar but increased in size to 1 to 2 mm. on agar containing certain enriching substances. Growth could be stimulated by the addition of large amounts (20 to 30 per cent) of blood plasma, whole blood and ascitic fluid or by the addition of small quantities (0.005 to 0.1 per cent) of sodium sulfite, sodium thiosulfate, sulfur, cystine and cysteine. Certain other sulfur compounds and also tryptophan, lysine and tyrosine failed to stimulate growth.

Fermentative capacities of the small forms were much the same as those of typical E. typhosa.

By absorption tests with antiserums, it was demonstrated that the small and large colony strains were serologically similar.

The small and large colony strains were equally effective in killing and protecting mice. The aberrant substrain 208 D was less virulent but afforded a high degree of protection against a normal strain.

The significance of the peculiarities encountered in these strains remains unexplained, and further investigation will be required.

TOOMEY, Cleveland [AUTHORS' SUMMARY].

THE DISTRIBUTION OF HEMOLYTIC STREPTOCOCCI GROUPS A, B AND C IN HUMAN INFECTIONS. LOWELL A. RANTZ and CHESTER S. KEEFER, J. Infect. Dis. **68**: 128 (March-April) 1941.

Eleven hundred and fifty-nine strains of hemolytic streptococci which were isolated from human beings were grouped serologically in order to determine the relative incidence of groups A, B and C in human infections. Of these strains, 1,104, or 95.2 per cent, were found to be group A; 19, or 1.6 per cent, were group B, and 14, or 1.2 per cent, were group C. Twenty-two strains were unclassified.

Group B hemolytic streptococci may occasionally cause septic arthritis, puerperal sepsis, bacterial endocarditis, peritonitis or pyelonephritis. They may be found as nonpathogenic organisms in the throat, vagina or skin. Occasionally they invade the blood as a terminal event in a chronic disease, such as chronic nephritis.

Group C hemolytic streptococci were not found to be the cause of infection in any of the cases studied. They were occasionally associated with other organisms in acute infections, but their significance could not be defined.

TOOMEY, Cleveland [AUTHORS' SUMMARY].

THE ELECTROCARDIOGRAM IN RHEUMATIC FEVER: A STUDY OF SYDENHAM'S CHOREA. ERNEST T. HEFFER, J. Pediat. **18**:363 (March) 1941.

The electrocardiograms of 181 patients in whom Sydenham's chorea was the first sign of rheumatic fever were studied. These patients were admitted to the hospital 250 times. Abnormalities were noted in 39 per cent of the electrocardiograms in the absence of clinical or other laboratory findings of cardiac involvement. The more significant of these abnormalities was the prolongation of the PR and QT intervals. The latter occurred in 18 per cent of the series, as compared with only 9.6 per cent of the former. Prolongation of both time intervals occurred in 8 per cent of the series. The electrocardiogram may corroborate a clinical diagnosis of rheumatic cardiac involvement and show the presence of active carditis.

RAUH, Cincinnati [AUTHORS' SUMMARY].

Chronic Infectious Diseases

REINFECTION IN CONGENITAL SYPHILIS. RICHARD D. HAHN, Am. J. Syph. Gonor. & Ven Dis. **25**:200 (June) 1941.

Two cases of reinfection in adequately treated patients with congenital syphilis are presented. Criteria of diagnosis for both the congenital and the acquired type were apparently rigidly fulfilled. The condition in each case doubtless was a true acquired type of syphilitic infection in a patient with congenital syphilis who had previously received adequate treatment.

REUTER, Milwaukee. [ARCH. DERMAT. & SYPH.]

A RAPID SLIDE FLOCCULATION TEST FOR SYPHILIS. FRANCISCO MARQUEZ, Am. J. Syph., Gonor. & Ven. Dis. **25**:319 (May) 1941.

In this article the author reports on the technic of a simplified rapid flocculation test for syphilis. A comparison with the Kahn standard test was made in 1,496 cases, and the results, as listed in the article, are apparently as sensitive and as quick as those of the Kahn standard test. This technic has the advantage of being rapid, easy and inexpensive.

ROYSTER, University, Va.

STUDIES IN TUBERCULOSIS. R. WEBSTER, M. J. Australia **1**:661 (May 31) 1941.

Webster is convinced that the bacteriologic diagnosis of tuberculosis by cultural methods is at least as effective as that by guinea pig inoculation. Inasmuch as the cultural method is cheaper, quicker and more practical in the handling of large numbers of specimens than the inoculation method, it should be used as a routine in all health, hospital and sanatorium laboratories. The technical methods involved require no elaborate equipment, and Myobacterium tuberculosis should receive the same treatment as diphtheria bacilli, meningococci and other pathogens of everyday occurrence which when not evident in a film preparation of suspected material are immediately subjected to appropriate measures for their cultivation.

GONCE JR., Madison, Wis.

THE ADEQUATE DIAGNOSIS OF INFANTILE CONGENITAL SYPHILIS. NORMAN R. INGRAHAM JR., BERTRAM SHAFFER, BARBARA E. SPENCE AND JAMES H. GORDON. Arch. Dermat. & Syph. **43**:323 (Feb.) 1941.

A five year follow-up study of 230 infants of syphilitic mothers is presented for the purpose of determining the accuracy of the diagnostic methods employed for the detection of infantile congenital syphilis in the light of recent advances in the knowledge of serologic and roentgenographic interpretation.

It is suggested that the use of roentgenograms as a subsidiary diagnostic aid will be of greatest value when it is reserved for the study of an infant whose mother has had a recent infection or a grossly insufficient amount of antepartum treatment, which renders the presence of the disease in the offspring most likely.

The quantitative titered Wassermann test seems to have its greatest value in detecting nonsyphilitic infants with positive serologic reactions at birth. In the present series 74 per cent of the infants presenting positive serologic reactions during the immediate neonatal period (up to fourteen days postnatally) apparently did not have syphilis.

The detection of the syphilitic infant by the use of the quantitative titered Wassermann test alone is complicated by the following facts. First, the birth of a syphilitic infant whose serum reagin titer is significantly greater than that of the mother is apparently an infrequent occurrence; second, the syphilitic as well as the nonsyphilitic infant may occasionally exhibit initially a decreasing titer; third, a significant rise in the serum reagin content may not occur for from four to eight weeks postnatally.

The most accurate diagnosis of infantile congenital syphilis would still seem to call for a close coordination in the interpretation of serologic reactions of the blood and roentgenographic changes.

JACKSON, Iowa City [AUTHORS' SUMMARY].

NEW METHOD FOR STAINING TUBERCLE BACILLI. V. HELLBERG, Acta med. Scandinav. **108**:12, 1941.

The staining solution consists of 0.2 cc. of 10 per cent potassium hydroxide dissolved in 100 cc of distilled water to which 2.5 cc. of liquefied phenol is added, followed by 10 cc. of 5 per cent alcoholic solution of Grübler's *Nachtblau*.

The slide is well covered with this solution and then carefully heated to slight boiling. The stain is allowed to act for five minutes, during which period the slide will have time to cool. The stain is poured off, and the slide is decolorized with 70 per cent alcohol which contains 3 cc. of 25 per cent hydrochloric acid in each 100 cc. until blue clouds cease to be given off. The slide is washed well with distilled water and then counterstained for five to ten seconds with a 0.1 per cent aqueous solution of neutral red containing 0.2 cc. of 1 per cent acetic acid in each 100 cc. It is then rinsed well with water and dried. The Koch bacilli stain dark blue.

The virtue of the stain is that it does not stain other micro-organisms occurring in expectorations except a yeast-oidium-like fungus. KAJDI, Baltimore.

Diseases of Blood, Heart and Blood Vessels and Spleen

ACUTE MASTOIDITIS COMPLICATED BY SCHÜLLER-CHRISTIAN DISEASE. KEMP G. COOPER, Arch. Otolaryng. **33**:1028 (June) 1941.

The author presents the case of a 3 year old child in whom the unusual combination of an ordinary pyogenic infection and a rare metabolic disturbance effecting the bones of the skull was found. Recovery followed surgical intervention and subsequent roentgen therapy. GREENWOOD, Chicago.

A HUMAN SERUM CONTAINING FOUR DISTINCT ISOAGGLUTININS. ALEXANDER S. WIENER and SAMUEL FORER, Proc. Soc. Exper. Biol. & Med. **47**:215 (June) 1941.

Because a female patient had hemolytic reactions following the transfusion of apparently compatible blood, study was made of the serologic reactions. The blood belonged to group O, type N, and agglutinated each one of 28 consecutive group O bloods, but no autoagglutinin was present. Two different irregular isoagglutinins could be closely identified. Three subsequent transfusions from 2 different donors of type ONRh—were successful. HANSEN, Minneapolis.

BLOOD PYRUVIC ACID IN HEART DISEASE. ZALE A. YANOF, Proc. Soc. Exper. Biol. & Med. **47**:516 (June) 1941.

The blood pyruvic acid level was found to be elevated in 20 patients with various degrees of congestive heart failure as compared with 10 normal subjects and 12 patients with heart disease but not decompensated. The increase in blood pyruvic acid approximates the degree of heart failure. HANSEN, Minneapolis.

ENTERORRHAGIA IN HEMOCYTOBLASTIC LEUKEMIA. A. CASTELLANOS, H. CALZADILLA, E. G. CONESA and S. BARRERAS, Arch. de med. inf. **10**:79 (April-June) 1941.

This clinical report is of a child with congenital syphilis in whose case the symptoms were bleeding from the intestine and an epileptic crisis. Hemograms and myelograms indicated a condition of hemocytoplastic leukemia.

SANFORD, Chicago.

A Case of Sickle Cell Anemia. Ortiz Machedo and Arostegui de la O., Arch. de med. inf. **10**:103 (April-June) 1941.

The child had 17 per cent sickle cells. Hemograms of the father, the mother and 2 brothers of the child showed no sickle cells, but by the Beck-Hertz technic all but 1 brother showed signs of sickling. Sanford, Chicago.

Hyperemic Splenomegaly, Intensified Hemolysis and Increased Fibrinogen Content and Sedimentation Rate of Red Blood Cells. E. Fagerberg, G. E. Fagerberg and R. Fåhraeus, Acta med. scandinav. **108**:1, 1941.

The authors produced hemolysis in rabbits by intravenous injection of distilled water or lysolecithin. A fall of the red cell count and an increase of fibrinogen and of sedimentation rate were observed. Similarly, ligation of the pancreatic duct caused a fall in the red cell count with a rise in the fibrinogen content. When the red cell count was raised by injection of homologous red blood cells, an increase of fibrinogen was noted.

The authors call attention to the fact that during pregnancy enlargement of the spleen is accompanied by destruction of blood, increased fibrinogen content and augmented sedimentation rate.

In newly born infants the spleen enlarges in the first five days and the red cell count falls, while the fibrinogen content and the rate of sedimentation increase.

In most infectious diseases (typhoid is among the few exceptions) active hyperemic enlargement of the spleen is found, with decrease of the red cell count and the fibrinogen content. Kajdi, Baltimore.

Diseases of Lungs, Pleura and Mediastinum

Multiple Pneumococcus Infections in Pneumonia. Sarah L. Cockrell and J. M. Ruegsegger, J. Infect. Dis. **68**:33 (Jan.-Feb.) 1941.

A case of pneumonia is presented in which six different pneumococci were typed from the sputum (types I, IV, VI, XI, XVI and XXI). Emphasis is placed on the importance of cultures of material obtained by lung suction as the best means of determining the exact cause of the pneumonia when multiple types are obtained from the throat. Toomey, Cleveland [Authors' Summary].

The Diagnosis and Conservative Treatment of Bronchiectasis in Children. Beryl E. Barsby and Richard E. Bonham-Carter, Arch. Dis. Childhood **16**:95 (June) 1941.

This paper gives in detail the anatomy of the bronchial tree in relation to the technic of bronchography. This technic consists in preparation of the patient by emptying the bronchi. This is achieved by postural drainage for eighteen hours daily for one week. The introduction of the contrasting oil is carried out by having the patient in the right position for filling the bronchi in the various lobes. Postural drainage is obtained by a special jacket with a built-in wedge which aids in maintaining the proper posture to allow drainage from the various lobes.

Kelly, Milwaukee.

A Survey of Primary Infantile and Juvenile Pneumonia. Mountjoy Elliott, Arch. Dis. Childhood **16**:121 (June) 1941.

A review of 895 cases of juvenile pneumonia that occurred in Dublin in the years 1937 to 1939 is given. The age of the patient and the type of causative organism are still of great importance in determining prognosis. There appears to have been a lowering of the death rate from atypical pneumonia in the first year of life since the introduction of chemotherapy, but the results in treating lobar

pneumonia in infants by chemotherapy alone are disappointing. Statistical and experimental studies suggest that the administration of serum with chemotherapy in cases of infantile pneumonia gives the best results. Experiments indicate that the antipneumococcic immunity mechanism is relatively weak in infants. Children over 2 years of age with pneumonia can be treated in the same manner as adults. All infants under 2 years of age with pneumonia should be treated in a properly equipped hospital. Blood transfusion, parenteral fluids, oxygen, sedatives and skilled nursing are almost as valuable as chemotherapy in cases of severe pneumonia in infants. They are particularly important for premature and poorly nourished children. The importance of maintaining weight during treatment is emphasized; efforts to continue breast feeding should be made.

KELLY, Milwaukee.

A CASE FOR DISCUSSION, WITH SPECIAL ALLUSION TO CONGENITAL ABSENCE OF LUNG. D. G. MADIGAN, Tubercle **22**:144 (June) 1941.

The case described was that of a woman aged 23 years who complained of pain near the inferior angle of the left scapula, unproductive cough and slight dyspnea on exertion. In appearance she was perfectly healthy. The physical findings were shrinking of the left side of the thorax and resonance on percussion over the anterior portion of the left side of the chest to the midaxilla, with dulness beyond this line. Normal breath sounds were heard as far laterally as the midclavicular line; no sounds were heard in the axilla, and tubular breathing was present posteriorly at the site of pain. Normal vesicular breathing was absent in the posterior left hemithorax. The brachial and radial pulses were weaker in the left arm, and the blood pressure on this side was correspondingly low.

Roentgen examination revealed reduced dimensions of the left side of the thorax and almost complete opacity to the rays. The mediastinal structures were displaced toward the left. The right lung appeared emphysematous. Injection of iodized poppyseed oil demonstrated a left main bronchus dividing into upper and lower branches and an elongated vertical sac laterally. Canalization of the smaller bronchi and alveoli had not occurred. Bronchoscopic examination showed the left main bronchus and its main divisions to be patent, but the mouths of the visualized bronchi were abnormally small.

From the history it appeared that pulmonary fibrosis and massive collapse could hardly have produced this condition. Bronchial occlusion, either from obstruction from without or from pressure from within, was ruled out by bronchography and bronchoscopy.

The diagnosis of congenital absence of the lung is suggested but cannot be irrefutably proved ante mortem.

EUGENE SMITH, Ogden, Utah.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

DIET IN MALNUTRITION AND CELIAC DISEASE, WITH SPECIAL REFERENCE TO THE USE OF DEXTROSE AND BANANAS. GENEVIEVE STEARNS, C. P. JEANS, RUTH CATHERWOOD and JOHN B. MCKINLEY, J. Pediat. **18**:12 (Jan.) 1941.

Four types of diets were used in a study of gain in weight in undernourished children, viz., the customary hospital diet, designated the "normal" diet, a diet richer in fat, called the "fat" diet, and a diet low in both fat and complex carbohydrates, containing its calories as protein and dextrose, called the "dextrose" diet. In the fourth diet ripe bananas were substituted for an equivalent amount of dextrose. Gains in weight were more rapid with the dextrose and banana diets than with either of the other two. Consistent gains in weight were obtained with the dextrose and banana diets and a lower caloric intake than with the other diets. The fat diet necessitated the largest caloric intake in order to maintain consistent gain in weight. The rapid early gains observed with banana and dextrose diets, presumably due in large part to water retention, were not subse-

quently lost but were apparently replaced by tissue gains without an intervening period of slow or no gain. The studies of retention of calcium, phosphorus and nitrogen confirmed the results of the studies of the gain in weight and showed that diets made up of protein and simple carbohydrates provide intake levels of these substances such that good body tissue can be built rapidly. These studies provide proof that the spectacular gains in weight observed are due primarily to sound tissue growth and that the resulting normal weight is an indication of normal body composition and is not due to inordinate amounts of fat or water.

RAUH, Cincinnati [AUTHORS' SUMMARY].

THE HIPPURIC ACID LIVER FUNCTION TEST IN CHILDREN. S. LONDE and J. G. PROBSTEIN, J. Pediat. **18**:371 (March) 1941.

Three grams of sodium benzoate is sufficient for gaging the maximum rate at which the liver can synthesize hippuric acid in children whose ideal weights for height and age range from 20 to 40 Kg. The adult dose of 4 Gm. is necessary for children whose ideal weights are 40 Kg. or over. Twenty-five control subjects, with ideal weights of from 20 to 40 Kg., receiving 3 Gm. of sodium benzoate, eliminated from 67 to 88 per cent in four hours, with an average of 79 per cent. Twenty-two of these subjects excreted from 32 to 58 per cent during the first two hours, with an average of 46 per cent. Ten control subjects, whose ideal weights were 40 Kg. or over, ingested 4 Gm. of sodium benzoate and excreted from 69 to 92 per cent in four hours, with an average of 82 per cent. For the first two hours these children eliminated from 41 to 74 per cent, with an average of 52 per cent. Tests were performed on 15 children admitted to the hospital for tonsillectomies. Nine of these subjects gave low values. Disturbed function was demonstrated in 2 children with chronic arthritis, in 2 children recovering from acute infections of the upper respiratory tract, in 1 with aniline dye poisoning and in 1 who had had a nephrectomy for a Wilms tumor of the kidney. Three of 4 patients with catarrhal jaundice had impaired hippuric acid functions. In children recovered from catarrhal jaundice the hippuric acid test gave normal results. Disturbed hepatic function was found in 2 of 3 subjects suffering from Banti's disease and in 1 case of gargoylism.

RAUH, Cincinnati [AUTHORS' CONCLUSIONS].

SURGICAL TREATMENT OF CONGENITAL PYLORIC STENOSIS. DAVID LEVI, Brit. M. J. **1**:963 (June 28) 1941.

The author describes and lists 100 cases of breast-fed babies who were operated on for congenital pyloric stenosis with no deaths. These were consecutive breast-fed babies, 13 girls and 87 boys. Forty-eight of the 100 babies were below birth weight when operated on. He compares with these results those of operations on 46 bottle-fed babies, in which there were 5 deaths. He points out the common features in the histories of all of the 5 children that died, pointing out that all 5 had presented feeding problems for one cause or another. The author states that "prolonged pre-operative preparation is neither necessary nor of great value. The administration of large quantities of saline subcutaneously and intravenously is not advised." He suggests that fluids are best taken by mouth and that the sooner the child can be placed in a position whereby it can benefit by fluid given by mouth the better the situation; he therefore recommends prompt operation.

ROYSTER, University, Va.

PRIMARY PNEUMOCOCCAL PERITONITIS. S. N. SEN, Indian J. Pediat. **8**:87 (April) 1941.

Pneumococcic peritonitis is a rare disease in India. It occurs mostly in girls, either as a primary infection or secondary to obvious infection elsewhere. The disease begins abruptly with abdominal pain, vomiting, diarrhea and fever. The

usual signs of peritonitis are present, but the boardlike rigidity may not occur for several days. If the acute stage is survived, a chronic stage develops during which it resembles "status typhosus" with later suppuration. It must of course be differentiated from other types of peritonitis and acute abdominal lesions. The prognosis is grave but improves if the patient survives the acute stage. The treatment is largely symptomatic and supportive, surgical intervention being reserved for the stage of localization. Chemotherapy and serotherapy have not been used enough to be evaluated.

TENNEY, Madison, Wis.

DERMOID CYST OF THE TRANSVERSE MESOCOLON IN A CHILD OF FIVE MONTHS. R. V. DIAZ, B. S. SANTIAGO and D. S. BENS, Arch. de med. inf. **10**:86 (April-June) 1941.

The symptoms were vomiting and distention. Surgical exploration disclosed a dermoid cyst.

SANFORD, Chicago.

Nervous Diseases

DILANTIN SODIUM THERAPY IN EPILEPTIFORM SEIZURES OF CHILDREN. E. C. LOWRY, Journal-Lancet **61**:178 (May) 1941.

Lowry used dilantin sodium in the treatment of epileptiform seizures of 34 children from 5 months to 16 years of age. The children were placed on a water restriction diet (900 cc. a day). The dosage of dilantin ranged from 0.2 to 0.4 Gm. daily, depending on the age and the tolerance of the child. Twenty-four had grand mal attacks, 2 had petit mal and 8 had seizures of both types. Two thirds of the children were treated for one year or more and one fifth for two years or more. The following results were obtained: Three children had complete cessation of seizures; 19 were improved (5 only moderately), and 12 were not benefited. In many the attacks became milder. The 65 per cent of favorable results is comparable to the experience of most workers, but some have reported a higher percentage of complete remissions. In all but 1 (whose seizures ceased) of the 23 children who received dilantin sodium continuously for a year or more the benefit was maintained throughout the period of observation without any increase in dosage, indicating that in general children do not acquire a tolerance for the drug. Most of the patients felt no ill effect from the medication. Patients with the most frequent attacks were most benefited. Phenobarbital and dilantin sodium were given to patients whose response to the latter medicament was unsatisfactory, and enough of these children improved to suggest that the combination is worth trying when other methods fail.

J. A. M. A.

MENINGITIS DUE TO SALMONELLA SUIPESTIFER. G. M. LYON and T. G. FOLSOM, West Virginia M. J. **37**:249 (June) 1941.

Lyon and Folsom report a case of meningitis due to an unusual small motile gram-negative rod treated with sulfanilamide. Two weeks before admission to the hospital a boy 2½ years of age became suddenly ill with fever, vomiting, malaise and diarrhea. From the parents it was learned that there had been a considerable amount of raw pork in their kitchen for two or three weeks preceding the apparent onset of his illness. There is much reason to believe that the meningitis and the bacilluria were caused by one of the Salmonella group, probably Salmonella suipestifer (the bacillus of hog cholera) rather than Salmonella schottmülleri (paratyphoid B bacillus). Either S. suipestifer infections in man occur infrequently or they are not recognized. The young seem to be more frequently affected, and while in them the infections are believed to be mild, the most severe form is also encountered in the very young. With all the Salmonella-contaminated raw pork

sold and taken into homes there have been relatively few illnesses traceable to S. suipestifer. This can best be explained on the basis of (1) the low pathogenicity of the organisms for man and (2) the failure to suspect the real causal agent. More careful bacteriologic study of the gram-negative bacilli encountered clinically would probably show a larger incidence of these infections than is generally recognized. Just what role sulfanilamide played in the management and recovery of the authors' patient is not clear. It is possible that he may have recovered spontaneously. However, it is the authors' impression that the drug was directly responsible for the recovery. They also believe that relatively high levels of the drug in the blood and the cerebrospinal fluid are required, as their patient did better clinically with high levels (from 18 to 24 mg. per hundred cubic centimeters) than with low levels (from 12 to 18 mg.). He also did better on combined oral and intrathecal administration than on oral therapy alone. At no time was there any significant evidence of toxicity other than a grayish discoloration of the skin. The authors know of no similar instance in which meningitis and bacilluria caused by a motile gram-negative bacillus were treated with sulfanilamide. Material was taken directly from the puncture needle for culture in nutrient broth. After from forty-eight to seventy-two hours a gram-negative bacillus possessing motility was observed. The bacilli were not agglutinated by serums which agglutinated the typhoid bacillus (Eberthella typhi), the Flexner dysentery bacillus (Eberthella paradysenteriae), the bacillus of paratyphoid A (Salmonella paratyphi) or the bacillus of paratyphoid B (S. schottmülleri Seiffert). In spite of the fact that the small gram-negative bacillus did not regularly satisfy all the cultural and fermentation characteristics of S. suipestifer, it seemed, on purely bacteriologic grounds alone, that the organism belonged more nearly to the Salmonella group than to any other. The finding of this motile gram-negative bacillus in cerebrospinal fluid and in the urine is of particular interest. Broth cultures from the blood gave no certain evidence of bacillemia, although they were not taken until relatively late in the clinical course and after chemotherapy was instituted.

J. A. M. A.

Psychology and Psychiatry

FACTORS ASSOCIATED WITH CRYING IN YOUNG CHILDREN IN THE NURSERY SCHOOL AND THE HOME. CATHERINE LANDRETH, Child Development **12**:81 (June) 1941.

Eight weeks' observation of 32 children in the nursery school and 25 of the same children in the home furnished data for an analysis of the factors associated with crying in young children in home and school situations. Correlation of the order of .5 indicated that children who habitually slept more than the group average cried more; that children with more health upsets cried more than those with few or none, and that children whose parents took them on simple trips and offered them a greater range of experiences cried less than those with a more limited daily routine. Chronologic age, length of nursery school attendance, irregularities of bladder control and irregular bowel elimination show no significant relationship with the percentage of time spent crying. In the school, 75 per cent of the crying was associated with conflicts between children; in the home 40 per cent arose from difficulties in establishing health routines of eating, sleeping, eliminating, washing and dressing. Twenty-one per cent of crying in the home arose from conflicts with adults, as against 5 per cent in the school. Definite sex differences were apparent in the boys, a greater percentage of incidents arising from conflicts with nursery school teachers and from frustration by inanimate objects. Boys were also more frequently associated with other children's crying than girls, the frequency ratio being 3 to 1. In conclusion, observation of this form of behavior in the nursery school gave only a partial picture of its significance for individual children.

AUTHOR.

THE MEASUREMENT OF PARENT BEHAVIOR. HORACE CHAMPNEY, Child Development **12**:131 (June) 1941.

This article describes the Fels parent-behavior rating scales, a battery developed in the Fels Fund longitudinal study of prenatal and postnatal environment. The scales are designed for the use of the home visitor in appraising the child's psychologic environment in terms of thirty variables which were selected in a previous study. The problems of measurement, rating scale format and scaling technic are discussed at some length. Parent-child behavior is held to be too complex to be handled by a simple, objective approach. The perceptual and integrative powers of the home visitor must be utilized and provided with an instrument for quantitative expression, and the rating scale is considered to be ideal for this purpose if it can be made sufficiently accurate. Several arguments are presented to indicate that the rating method has greater potentialities than have usually been recognized, and a number of procedures are proposed for the construction of optimally refined scales to be used by trained raters. A "graphic-parallel-vertical" format is described, employing "behavior cues" which have been scaled by a method employing the graphic judgments of experts. Certain criteria for good cues are formulated, and several supplementary ratings are proposed as a means of promoting more careful rating. A statistical report on reliability, validity and norms is left for a later paper.

AUTHOR.

WHO IS CAPABLE OF TREATING PSYCHIATRIC PROBLEMS OF CHILDREN? JULIUS SURANYI, Ztschr. f. Kinderpsychiat. **8**:1 (May) 1941.

The author, a pediatrician, mentions two aspects of the problem: first, the hesitancy of the pediatrician to recognize the existence of psychologic problems of the child; second, the difficulty and opposition on the part of parents in seeking the necessary treatment for such problems. The author comes to the conclusion that the physician who is interested in, and feels capable of supplying advice regarding, the problems of his young patients must further equip himself with recent knowledge in the application of psychologic principles. The pediatrician, on the other hand, who is not conversant with psychiatric methods should consider it his duty to find such care for the child elsewhere among his colleagues. The author further expresses the hope that in the future the pediatrician will devote as much time to the study of mental and emotional phases as he has to the physical growth and development of the child.

JAHR, Omaha.

A TEST FOR THE EXAMINATION OF THE SOCIAL STATUS OF THE CHILD AND THE ADOLESCENT. FRANZISKA BAUMGARTEN TRAMER, Ztschr. f. Kinderpsychiat. **8**:11 (May) 1941.

The test consists of twelve charts, six of which indicate positive social action (the child leading a blind man across the street; a child helping another child, etc.) and six negative acts (a child fighting with his fellow; a child interfering with another's play, etc.). The subject to be examined is asked to interpret the pictures. The manner in which the answers are given as well as the contents of the replies are recorded, and other pertinent remarks submitted in connection with the answers are also entered. An analysis of these replies taken together with other personal factors, the author believes, offers a workable index to the social experiences and the disposition of the youngster under consideration.

JAHR, Omaha.

Diseases of the Genitourinary Tract

FURTHER OBSERVATIONS ON GONOCOCCAL VULVOVAGINITIS. ALFRED COHN, ARTHUR STEER and ELEANOR L. ADLER, Am. J. Syph., Gonor. & Ven. Dis. **25**:329 (May) 1941.

This article is a review of the case histories of 234 patients having gonococcic vulvovaginitis. It consists mainly of charts and figures showing the clinical

course under various types of treatment. The authors state definitely that cultures were found to be greatly superior to smears in making the diagnosis. They reported that 38 per cent of rectal cultures taken during the acute stage of the vaginitis were positive but that they became negative spontaneously. The authors found that gonococcic infection occurred in about 50 per cent of the families in which cases were reported and they thought that the relationship between the child and the infected adult must be quite intimate if the child became infected. However, they state "infection of one child by another through the medium of toilet seat would appear to be rare." It was thought, however, that the towels and linens contaminated with gonococcic pus could be a factor in the transmission of the vaginitis. In this series of cases spontaneous cures in untreated patients occurred in 78.8 per cent by the twenty-fifth week of observation.

The patients treated with estrogenic substance showed only slightly better results than those receiving no treatment at all. However, it was observed that the external discharge disappeared sooner in the patients treated with estrogen than in those not treated. Sulfanilamide gave approximately 50 per cent cures in the outpatient department and 68 per cent cures in the hospital. It was noted that prolonged or repeated treatment did not increase the number of cures.

Sulfapyridine was used, and in every instance the vaginal culture taken after the onset of treatment was negative. It was said, however, that 10 per cent of the blood cultures of these children became positive in from sixteen to thirty-two weeks after therapy. About 50 per cent of the patients who began having a positive smear seemed to be suffering from a new infection and 50 per cent seemed to have had a recurrence. It was noted that about a fifth of all the patients seen acquired the carrier state, in which an occasional positive culture occurred in the absence of clinical signs even after twenty-eight weeks of observation.

ROYSTER, University, Va.

PROPAGATION OF THE VIRUS OF LYMPHOGRANULOMA VENEREUM ON THE CHORIOALLANTOIS OF THE DEVELOPING EGG. MARION E. HOWARD and WINIFRED S. HULL, J. Infect. Dis. **68**:73 (Jan.-Feb.) 1941.

The virus of lymphogranuloma venereum was propagated on the chorioallantoic membrane of the developing egg. Success was dependent on several factors. The time of egg membrane transfers greatly influenced the results obtained. Infectivity of membranes could best be demonstrated by early passage. Antigenicity as measured by the Frei test in man seemed in many instances to be highest when infectivity had passed.

TOOMEY, Cleveland [AUTHORS' CONCLUSIONS].

THE TREATMENT OF GONOCOCCAL VULVOVAGINITIS IN CHILDREN: A REPORT OF EIGHTEEN CASES TREATED BY THE IMPLANTATION OF ESTRADIOL BENZOATE. JOHN W. HOLMES, J. ALBRIGHT JONES, NATHAN H. EINHORN and LOUIS A. WIKLER, J. Pediat. **19**:70 (July) 1941.

Eighteen children with gonococcic vulvovaginitis were treated with estradiol benzoate by implanting a pellet representing 90,000 international units in the fat of the buttock. Within an average of eight and three-tenths days after the implantation squamous epithelial cells began to appear. Within an average of thirteen and six-tenths days after the implantation all patients showed squamous epithelial cells and negative smears for the gonococcus. No recurrences of the infection have occurred to date. One patient had slight vaginal bleeding on two occasions. Four others showed moderate enlargement of the breasts, and 1 of these had a few pubic hairs.

RAUH, Cincinnati [AUTHORS' SUMMARY].

EXCRETORY UROGRAPHY FOR CHILDREN: INDICATIONS AND METHODS. GEORGE M. WYATT, Radiology **36**:664 (June) 1941.

It is obvious that an early diagnosis of an obstruction is essential if surgical intervention is to be effective. For this, descending urography has the advantage

of being a more physiologic, safer and less complicated procedure, rarely requiring anesthesia. Retrograde pyelography, when indicated and physiologically possible, may be used, but as a rule it should follow excretory urography. Infections of the urinary tract with retention symptoms after repeated attacks are indications for excretory urography. Though infection is less common in the male, it is more often associated with congenital malformations. Symptoms of obstruction may be misleading if unassociated with infection. Pain is often referred to the umbilicus; vomiting may be the only symptom, and roentgenograms may show the only sign. Other indications sometimes encountered are abdominal tumors, orthostatic albuminuria and congenital malformations of the external genitalia.

Excretory urography during early life presents problems seldom met with in adults, and satisfactory urograms are not to be obtained unless these difficulties are overcome. Most important are the accumulation of gas in the small intestine and poor concentration of urine.

Most of the gas in the small intestine represents swallowed air. The author proposed a method of preventing the air from reaching the intestine by not allowing it to reach the pyloric portion of the stomach. This may be accomplished by three optimum positions, which are: (1) upright, (2) prone with the head slightly elevated, and (3) on the right side. Supine and left-side-down positions are to be avoided for at least twelve hours before the roentgen examination. Any break in the technic almost immediately results in passage of air from the stomach into the small intestine. There is little trouble with gas in children over 5 to 8 year of age since these patients are usually able to stand and have an opportunity to pass air from the stomach by eructation. Pitressin has proved an aid in eliminating gas in children over 2 years of age (blood pressure should be watched). Enemas frequently introduce more gas than is expelled. Compound licorice powder as a cathartic is recommended for children over 2 years of age.

Poor concentration of urine is almost universal in children under 1 year of age, owing to their large fluid intake. While restriction of fluid is important, it should not be carried to the point of making the child cry, as crying increases the amount of air swallowed. It is better not to restrict the intake of fluids in very young infants and to increase accordingly the amount of diodrast administered.

Preparation for excretory urography should start at the time of the last evening feeding before the morning of the examination, and no break in the postural technic, even for an instant, should occur until the examination is completed. Bathing and weighing should be omitted.

The following are the instructions for children who can sit or stand alone:

(1) An effective cathartic should be administered the night before the examination unless contraindicated.

(2) The intake of water and of other fluids after 8:00 p. m. of the night preceding the examination should be limited, but not to the point of causing the child to cry.

(3) He should have a small breakfast—fruit, toast with butter, cereal with a small amount of cream and an egg. Small children should be given a few sips of milk or water.

(4) He should be allowed all the activity that is necessary to prevent crying.

Doses as high as 1 cc. of diodrast solution (35 per cent) per pound of body weight are necessary for younger infants. A satisfactory scale to follow is:

10 cc. for children under 6 months of age

15 cc. for children between 6 months and 2 years of age

20 cc. for children between 2 and 5 years of age

25 cc. for children over 5 years of age

Diodrast is administered intravenously, and all films are exposed with the patient in the upright posture.

ANSPACH, Chicago.

SULFATHIAZOLE AND SULFAPYRIDINE THERAPY IN URINARY TRACT INFECTIONS. E. P. ALYEA and C. STUART, South. M. J. **34**:993 (Sept.) 1941.

Alyea and Stuart state the belief that sulfathiazole has a higher therapeutic index for Staphylococcus and Streptococcus faecalis than sulfanilamide or sulfapyridine. It is less toxic for human beings and is excreted much faster and more completely than sulfanilamide and other derivatives of it.

Sulfathiazole is eliminated by the kidneys in direct proportion to their phenolsulfonphthalein excretion. Although a damaged kidney may excrete very little of the drug, it produces a concentration higher than one might expect. It does not produce, however, a concentration as high as the good kidney.

The authors found that sulfapyridine produced the highest percentage of cures for colon bacillus infections, and sulfathiazole the highest for staphylococcic infections. Doses of 3 Gm. the first day and 2 Gm. a day thereafter are recommended for sulfapyridine and sulfathiazole therapy of infections of the urinary tract. Specificity of drug response for various organisms should be emphasized.

SCHLUTZ, Chicago.

Diseases of the Eye

HEREDITARY CATARACTA CAERULEA. O. R. WOLFE and R. M. WOLFE, J. Internat. Coll. Surg. **4**:322 (Aug.) 1941.

The authors give—in three languages—the following summary of their report:

"Removal of soft cataracts by suction is an ideal method, as full restoration of vision is quickly obtained, it renders the usual needling operation obsolete and there is no disfigurement. Contact lenses can be comfortably worn after cataract surgery.

"Three cases of hereditary cataracta caerulea occurring in one family are reported. The condition was treated surgically in all three cases, with gratifying result."

W. ZENTMAYER. [ARCH. OPHTH.]

GONOCOCCAL CONJUNCTIVITIS IN CHILDREN: A COMPARISON OF TREATMENT WITH SULFANILAMIDE AND SULFAPYRIDINE WITH A NOTE ON SULFATHIAZOLE. LEWIS K. SWEET, J. Pediat. **19**:60 (July) 1941.

Sixty-two patients with gonorrheal conjunctivitis were treated with sulfanilamide or sulfapyridine. Forty-six were newborn infants, and 13 were older children. Of 30 treated with sulfanilamide, 24 showed rapid recovery. Thirty-three patients, including 4 who failed to respond to sulfanilamide, received sulfapyridine. A rapid recovery occurred in 31 patients. Two newborn infants and 1 older child were treated with sulfathiazole, and all responded promptly. In 1 patient treated with sulfanilamide a corneal ulcer developed. Very few complications resulting from toxicity of the drugs occurred. Sweet believes that sulfapyridine is superior to sulfanilamide in the treatment of gonorrheal conjunctivitis.

RAUH, Cincinnati.

DISTANCE OBJECT TEST TYPE FOR CHILDREN. F. E. PRESTON, Brit. J. Ophth. **25**:357 (Aug.) 1941.

Preston has constructed a test type chart on the strictly Snellen principle. An original test chart with thirty-two objects was printed and was tried out at school clinics in different parts of the country.

The objects retained are either easy to interpret or else capable of a varied interpretation, so that the test is an estimate of the child's visual acuity and not of his intelligence. The author recognizes that the same principle has been used before in the construction of test types for children.

W. ZENTMAYER. [ARCH. OPHTH.]

SPECIAL CASE OF MELANOSIS FUNDI: BILATERAL CONGENITAL GROUP PIGMENTATION OF THE CENTRAL AREA. A. LOEWENSTEIN and J. STEEL, Brit. J. Ophth. **25**:417 (Sept.) 1941.

The authors describe first the atypical congenital pigmentation of the retina in which the grouped patches of pigment occupy a sector of the fundus. About 40 cases have been reported. All are similar, and all have the common feature that the central area is always free. A case of group pigmentation is described which according to the authors differs from all others published. The ophthalmoscopic picture was that of seemingly congenital pigment patches located at the central area, symmetric in both eyes, the patches being almost similar in shape and size and surrounded by a halo without reflex, dark by indirect illumination and grayish white by direct illumination. Some of the patches contained grayish white corpuscles, perhaps cysts.

The idea of an atavistic patchlike growth of Sattler's choroidal tapetum layer is mentioned, but it seems not impossible that the patches are provoked by nevus cell groups.

The article is illustrated. W. ZENTMAYER. [ARCH. OPHTH.]

Skin Diseases; Allergy

CONTACT DERMATITIS DUE TO UNDERWEAR: OBSERVATIONS IN FOURTEEN CASES WITH SUMMARY OF EFFORTS TO DISCOVER THE CAUSE. ARTHUR WRIGHT NEILSON and A. J. REICHES, Arch. Dermat. & Syph. **44**:218 (Aug.) 1941.

Fourteen male adolescent patients were observed with contact dermatitis caused by wearing unwashed shorts. The condition started after the patients had worn the shorts for at least forty-eight hours and consisted of sharply demarcated dermatitis covering the lower part of the back, buttocks and thighs. Edema with associated pain and pruritis about the genitalia was a constant feature. The cause was investigated and was found to be a commercial oleoresin used in finishing the cloth.

JACKSON, Iowa City.

INTERTRIGO (CHAFING) TREATED WITH TANNIC ACID AND BRILLIANT GREEN. LOUIS TULIPAN, J. A. M. A. **116**:1518 (April 5) 1941.

Patients with various types of intertrigo were treated by tannic acid spray when there was no superimposed infection or by tannic acid combined with brilliant green when infection was present. The author's results seemed better than any produced by the usual powders, ointments or compresses.

HEERSMA, Kalamazoo, Mich.

AMINO ACIDS AS A SOURCE OF NITROGEN FOR ALLERGIC INFANTS. LEWIS WEBB HILL, J. A. M. A. **116**:2135 (May 10) 1941.

Clinical application of the use of an amino acid–containing food substitute for milk was carried out on 36 infants. In more than half of the cases improvement occurred, and the preparation was tolerated well. Since no preparation is entirely satisfactory as a substitute for milk in infants with eczema, several types of substitute are available; and this one is tolerated especially well by the digestive system of very young infants.

HEERSMA, Kalamazoo, Mich.

SKIN TESTING METHODS: MULTIPLE SINGLE SITTING VS. SERIAL SMALL GROUP TESTS. OSCAR SWINEFORD JR., J. Allergy **12**:470 (July) 1941.

Eighty to 120 intradermal tests were done on 2,018 patients. Scratch tests were done on each patient before the intradermal tests. Only 64 of the 2,018 had negative reactions; 335 had more than 30 positive reactions. Only 2 patients had

systemic reactions. One of these had a marked local reaction to ragweed; the other had severe local reactions to crabs and shrimps.

Two other patients, not in this group, had systemic reactions when tested intradermally with but one antigen.

The authors feel that multiple intradermal tests are no more dangerous than a few tests at a sitting and that numerous simultaneous average positive reactions do not cause systemic reactions by their cumulative effects.

HOYER, Cincinnati.

HYPERSENSITIVITY TO BEETLES (COLEOPTERA): REPORT OF A CASE. J. M. SHELDON and J. H. JOHNSTON, J. Allergy **12**:493 (July) 1941.

Sheldon and Johnston report on a case of asthma believed to be due to emanations from beetles. The patient was a museum curator.

HOYER, Cincinnati.

WATER FLEA SENSITIVITY: CASE REPORT. KARL D. WAY, J. Allergy **12**:495 (July) 1941.

Way reports a case of asthma in a man who raised tropical fish as a hobby. Fish foods containing the water flea were found to be the offending substances.

HOYER, Cincinnati.

A CASE OF VON RECKLINGHAUSEN'S DISEASE WITH DIFFUSE NEUROFIBROMATOSIS OF THE CHOROID. S. ROBSON and W. BLACKWOOD, Brit. J. Ophth. **25**:431 (Sept.) 1941.

The patient was a boy aged 10 years. For four years the upper lid of the right eye was thickened and pendulous. Wormlike swellings could be felt beneath the skin, extending above the eyebrow. Movable swellings were present on the front of the right side of the neck, on the abdomen in the course of the intercostal nerves, in the left groin and on the front of the left shoulder. There was a large café au lait patch on the left buttock, and there were smaller ones on the abdomen and the back. Later innumerable café au lait spots covered the back and abdomen.

The right eye showed a large detachment of the retina. The eyeball was removed. Histologic study of biopsy specimens from the head and neck showed neurofibromatosis.

Microscopic examination of the optic nerve, optic disk, retina and sclera showed no particular abnormality. The choroid was generally thickened, with a focal accentuation of the thickening. The central tumor contained well formed adult nerve cells, each with a characteristic nucleus and nucleolus. These cells lay in little groups, and between the groups ran whorls and "bundles," which contained myelinated nerves. The "bundles" had the same histologic character as those of the central tumor. The long ciliary nerves running within the substance of the choroid showed no abnormalities. Myelinated nerve fibers were found within the substance of the "round or ovoid bodies." The ovoid bodies were the result of transverse sections of the neurofibromatous bundles which formed the main mass of the tumor. The tumor was only moderately vascular, the blood vessels being well formed and healthy.

In summary the authors say:

"A case of von Recklinghausen's disease has been described with diffuse neurofibromatosis in the course of the short ciliary nerves.

"The histological appearances were similar to previous cases in the literature, including the presence of 'ovoid or round bodies.'

"It has been possible to demonstrate nerve fibers in the 'ovoid or round bodies' and it is suggested that these 'ovoid bodies' are a normal constituent of a diffuse neurofibromatosis."

The article is illustrated. W. ZENTMAYER. [Arch. Ophth.]

A SMALL EPIDEMIC OF PUSTULOSIS VARIOLIFORMIS ACUTA. MARGRIT ESSER, Ann. pædiat. **157**:156 (Sept.) 1941.

The appearance and clinical course of the cases of a small epidemic of pustulosis varioliformis acuta are described.

The inoculated substance engenders in the rabbit's eye keratoconjunctivitis which can be reinoculated and produces immunity against a later inoculation of herpes. A herpes-like virus, which adheres to injured skin, is the cause of the eruption.

AUTHOR'S SUMMARY.

Miscellaneous

WASP STING AS AN IMMEDIATE CAUSE OF DEATH. S. C. DYKE, Lancet **2**:307 (Sept. 13) 1941.

Immediately fatal results, accompanied by the same chain of symptoms, have been reported after the stings of bees as well as of wasps. Two new cases are placed on record.

In all immediately fatal cases the victims show an identical chain of symptoms preceding death; within two minutes of the sting the person collapses, consciousness is lost and he dies within half an hour. Subjects surviving for half an hour may show severe symptoms of anaphylactic type but always recover.

No observations appear to have been made on the chemical nature or pharmacologic action of wasp venom. Bee venom is a highly complex substance including a volatile oil, tryptophan, choline, fatty acids and a water-soluble acid with a hemolytic effect. Contrary to current opinion, formic acid is not the active principle of the venom. It is present, but the venom retains its activity undiminished after this has been driven off.

Langer differentiated three separate toxic effects following the intravenous injection of the venom: neurotoxic, cytolytic (affecting endothelial cells) and hemolytic.

LANGMANN, New York.

CONCENTRATIONS OF SULFAPYRIDINE AND SULFATHIAZOLE IN THE BLOOD AND SPINAL FLUID. ENRIQUE G. CONESA and ALEJANDRO DEL FRADE MENESES, Arch. de med. inf. **10**:71 (April-June) 1941.

On the basis of 110 determinations during a twenty-one day period on a 6 year old boy with Haemophilus influenzae meningitis, the authors decided that variations in concentration were due to diuresis, hydration of the patient and dysfunction of the liver. The sulfathiazole did not pass to the spinal fluid in sufficient amounts to be of therapeutic value, while the sulfapyridine passed in sufficient amounts to reach values as high as 85 per cent of the blood value.

SANFORD, Chicago.

Society Transactions

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

T. G. H. DRAKE, M.D., *President*

Nineteenth Annual Meeting, Belleville, Ontario, Canada, June 6, 1942

First Session

Saturday Morning

Presidential Address. DR. T. G. H. DRAKE, Toronto.

Combination of Tetany and Decreased Kidney Function in the Newborn. DR. C. E. SNELLING, Toronto.

Eleven cases in which there were symptoms of tetany of the newborn are presented. The blood calcium level was lowered in most cases and the phosphorus level elevated. In every instance there was a decreased calcium-phosphorus ratio. In addition to the elevated phosphorus content, there were varying degrees of nitrogen retention. Such nitrogen-phosphorus retention is probably caused by disturbed renal function. The hyperphosphatemia interferes with the ionization of calcium, causing the symptoms of tetany. These symptoms were relieved in the cases reported by injection of calcium gluconate intravenously. Disturbed renal function is a cause of tetany of the newborn in some of the cases.

DISCUSSION

DR. A. P. HART, Toronto: I was rather impressed by the number of cases in which there was a history of difficult birth. Is this a factor in the production of the disease?

DR. N. SILVERTHORNE, Toronto: Two patients that I have seen with some or many signs attributable to cerebral hemorrhage also showed signs of tetany. Have you any explanation for this combination of symptoms?

DR. T. G. H. DRAKE, Toronto: I believe that in Dr. Ebbs's investigation, in which he was following pregnant women on poor and on good diets as regards calcium and vitamin D, tetany of the newborn occurred in 4 of the offspring of women receiving poor diets but in none of the offspring of women receiving good diets. Do you know whether calcium and phosphorus estimations were done in these cases?

DR. C. E. SNELLING, Toronto: With regard to Dr. Hart's question, Shannon was one of the first to describe the syndrome now known as tetany of the newborn. He diagnosed the condition on symptoms only. No calcium estimations were made in any of his cases. The syndrome followed difficult delivery, and he believed the symptoms of tetany were due to edema of the brain following trauma during birth. Later workers found that the symptoms were not always associated with difficult labor and found that the calcium levels were low. Dr. Drake recently suggested the following possible explanation: The babies often suffer from shock and intracranial hemorrhage as the result of the difficult labor, and consequently they do not feed well and they lack fluids. Because they are not taking sufficient fluids, their kidneys cannot excrete normally. Consequently, the phosphorus and nitrogen are retained and reach high levels in the blood. The ionized calcium in the blood is depressed as a result of the high phosphorus level. The total calcium is not necessarily reduced.

As for Dr. Ebbs's reports, I am not sure whether phosphorus determinations were made in his cases. The hematocrit reading for a newborn child is 65 to 75 per cent. In order to determine the blood phosphorus, calcium, nonprotein nitrogen and creatinine, one needs to remove a considerable amount of blood, and this is not always possible.

DR. T. G. H. DRAKE, Toronto: I believe that Dr. Snelling suggests that there are two types of tetany of the newborn. In the first type, there is a slight decrease in the blood calcium and an increase in the inorganic phosphorus. This is due to poor kidney excretion, which causes an increase in the blood inorganic phosphorus, which in turn depresses the level of the ionized calcium in the blood. In the second type, there is a greater decrease in the blood calcium, and the phosphorus is normal or slightly increased. These conditions are probably due to deficiencies in calcium and vitamin D in the mother's diet during pregnancy. The second type of tetany of the newborn can be prevented by an adequate antepartum diet. In the first type, the tetany of the newborn is due to metabolic disturbances in the baby.

DR. C. E. SNELLING, Toronto: This is the point that I was bringing out: that is, there is more than one type of tetany of the newborn.

Lesions Produced by Intrathecally Injected Sodium Sulfapyridine. DR. ELEANOR R. MACKENZIE (by invitation), Montreal, and DR. R. R. STRUTHERS, Montreal.

Three patients in whom unilateral flaccid paralysis developed after intrathecal injection of sodium sulfapyridine are presented. It is believed that the paralysis results from damage to the nerve roots by the excessive alkalinity of the drug. The pathologic picture is shown in 1 case to be a degeneration of the Nissl granules of the nerve cells.

DISCUSSION

DR. R. R. STRUTHERS, Montreal: We have been warned before of the danger of sulfapyridine when administered intrathecally, but the only report in the literature is in a French journal, a photostatic copy of which was secured from the Surgeon General's office. One drug firm in Montreal, which advertises among French physicians, states that this drug may be used intrathecally, although caution is advised. Dr. Mackenzie's paper is ample warning of the danger of administration of this drug intrathecally.

DR. T. G. H. DRAKE, Toronto: Dr. Mackenzie stated that she diluted the drug twenty-five times but that this caused very little change in the p_H, which was still alkaline. With what did she dilute it?

DR. E. R. MACKENZIE, Montreal: It was diluted with distilled water. It was not possible to obtain enough spinal fluid to dilute it with that.

DR. NELLES SILVERTHORNE, Toronto: I heartily agree that the derivatives of sulfanilamide should not be given intrathecally. In a few cases in which we injected them intrathecally, the spinal fluid became jelly-like in consistency, and we gave up this practice for that reason.

Meningitis in Childhood. DR. NELLES SILVERTHORNE, Toronto.

A study of the incidence of various types of meningitis is reviewed. The study embodies a survey of 1,100 histories of patients with meningitis for a period of twenty-two years, from 1919 to 1941. The results of newer methods of treatment of the different bacterial types are presented, and other factors in the treatment of and recovery from meningitis are discussed.

DISCUSSION

DR. H. S. LITTLE, London, Ontario: Would Dr. Silverthorne go so far as to state that in the vast majority of cases of meningococcic meningitis chemotherapy

alone is sufficient and that intravenous or intrathecal administration of serum is necessary only for the patients with fulminating meningitis or those that are drug fast? In many cases it is almost impossible to cultivate meningococci from the spinal fluid twenty-four hours after the administration of the drug. It would appear that the antiserum is not necessary in the great majority of cases of meningococcic meningitis. In regard to lumbar punctures, if one sees marked clinical improvement, would it not be advisable to discontinue their daily use?

DR. H. B. CUSHING, Montreal: At the last meeting of this society I spoke on meningococcic meningitis in children and I stated quite positively that I believed the meningococcus is extremely susceptible to the action of sulfonamide compounds. The modern treatment of this disease is therefore with these compounds only, and it is unnecessary to use serum in addition. The chemotherapy is better than any other. My experience since then has confirmed me in this belief. Sulfonamide compounds are used as the sole treatment of meningococcic meningitis in Montreal. Dr. Silverthorne described one patient who had a high level of the drug in his cerebrospinal fluid and a high temperature. In this case he stopped the drug and gave serum. Possibly the fever was due to the drug, and therefore its discontinuance relieved the fever rather than the serum. In regard to lumbar puncture, I advise it as seldom as possible. One cannot drain off the spinal fluid adequately. The amount of infected cerebrospinal fluid removed by a lumbar puncture is insignificant. Therefore, why subject the patient to frequent lumbar punctures?

DR. C. E. SNELLING, Toronto: At the present time, when one sees an acute infection, for example an acute infection of the respiratory tract, one gives the patient one of the sulfonamide compounds. Will this practice reduce the number of cases of meningitis? One child to whom I gave a fairly large dose of sulfathiazole showed purpuric spots three to four hours later and then all the symptoms of fulminating meningitis or meningococcemia. The child made a recovery with continued administration of the drug in large doses. If she had not received the large dose of this drug, might meningitis have developed?

DR. E. A. MORGAN, Toronto: I should like to ask Dr. Silverthorne to define what he means by "cure," especially with regard to streptococcic and influenzal meningitis. Does this mean a complete cure without sequelae?

DR. BENJAMIN BENJAMIN, Montreal: Dr. Silverthorne's figures for recoveries of patients with pneumococcic meningitis treated with sulfonamide compounds—if I remember correctly, 2 of 31 patients—are lower than any I have seen. Very young infants are likely to do badly, possibly because of poor response of the immunity mechanism. I treated a 6 week old baby suffering from this disease, but I was unable to save it. I wonder whether the ages of the children and the fact that the pneumococci present included a large number of highly virulent types had anything to do with the low recovery rate. Could Dr. Silverthorne also tell something about the concentrations of the drugs in the spinal fluids of the patients on whom he did frequent lumbar punctures?

DR. R. R. STRUTHERS, Montreal: Is there any correlation between the level of the drug in the spinal fluid and the likelihood of recovery? My impression is that there is no correlation, and I do not approve of daily lumbar punctures. It is essential to have one lumbar puncture for diagnosis and one after treatment is complete to see if the cerebrospinal fluid is still sterile. Lumbar puncture is a serious procedure for an infant. In regard to the route by which a sulfonamide compound should be given, in the last two years I have been giving the drug intravenously for the first forty-eight hours and then orally. The results following this procedure are more rapid and I believe better than those following oral administration alone, especially if the patient is in coma or in convulsions.

DR. NELLES SILVERTHORNE, Toronto: In reply to Dr. Little, most patients with meningococcic meningitis are treated with sulfonamide compounds alone in our hospital. We are using this method mainly now. We have not used these

drugs intravenously continuously. In certain isolated examples one should use polyvalent serum as well as the drug. In regard to the daily lumbar punctures, if the patient improves from day to day it is not necessary to carry out this procedure daily. However, frequent lumbar punctures are needed. I do not believe spinal fluid should be left undrained. For instance, in 2 cases of meningitis due to type I meningococci, the patients were given the drug for eight days, but the meningococci were persistently present in the cerebrospinal fluid. Then polyvalent antimeningococcus serum was given intrathecally, and immediately the cultures became sterile. Dr. Sara Branham has shown by laboratory tests that certain strains of meningococci will not respond to serum and certain others will not respond to chemotherapy. Some strains are killed only by a combination of chemotherapy and serum. In regard to Dr. Snelling's question as to whether it is possible to prevent the development of meningitis by treating infections of the respiratory tract with good doses of a sulfonamide compound, this would not appear to be likely, as meningitis may develop in patients suffering from pneumonia who have high levels of the drug in their blood. As for Dr. Morgan's question in regard to the cure of influenzal meningitis, intelligence tests were carried out on these patients some months or years after they were discharged as cured. All but 1 of them had normal intelligence quotients; 2 of them were deaf. In regard to pneumococcic meningitis, all of the strains that were typable were typed. A variety of types were found, including I, XVIII, V, VII and XIX. Even when the drug levels in the spinal fluid were as high as 4 to 22 mg. per hundred cubic centimeters, living organisms were found in it. I cannot agree that there is no correlation between the level of the drug and the number of bacteria in the spinal fluid. In 1 case, that of a 12 year old boy with type XVIII pneumococcic meningitis, the following sequence of events occurred. Cultures of his cerebrospinal fluid showed myriads of pneumococci. He was given 300 to 500 grains (19.5 to 32.5 Gm.) of sulfadiazine in twelve to twenty-four hours or 4 to 6 grains (0.26 to 0.39 Gm.) per pound daily. Lumbar puncture was done daily. In five days the spinal fluid was sterile, and his fever fell by crisis as in pneumonia. The level of sulfadiazine in the cerebrospinal fluid reached 10 mg. per hundred cubic centimeters. I have never seen lumbar punctures do any harm, and I believe they are valuable. I have had patients with meningococcic meningitis recover with less than 2 mg. per hundred cubic centimeters of the drug in their spinal fluid. Recovery is perhaps due to the patient's immunity as well as to the effects of the drug. The mortality rate in meningococcic meningitis is low. There are few organisms in the cerebrospinal fluid, and they are extremely sensitive to most of the sulfonamide compounds. If there are myriads of highly virulent meningococci in the cerebrospinal fluid, the patient will probably die. The meningococci vary greatly in their virulence: Sometimes they are so virulent that two organisms will kill a mouse in a virulence test, and sometimes it takes twenty thousand of the organisms to kill a mouse.

Acute Infectious Polyneuritis. Dr. H. B. Cushing, Montreal.

It has recently been generally accepted that there is such a disease as acute infectious polyneuritis, which was formerly and is yet commonly confused with poliomyelitis. It is believed to be due to a filtrable virus, but this has not been isolated.

The disease differs from poliomyelitis in both age and seasonal incidence, in the symmetry of the paralyses and in the more pronounced hyperesthesia. There is increase of albumin and globulin in the cerebrospinal fluid but no increase in cells (so-called albuminocytologic disassociation). The prognosis is good, and there is no residual paralysis. On account of the different treatment and outlook, the correct diagnosis is important.

DISCUSSION

Dr. Nelles Silverthorne, Toronto: In the epidemic of poliomyelitis in Toronto, patients were sent into the hospital with at least seven different condi-

tions diagnosed as poliomyelitis. These included osteomyelitis, tuberculous meningitis, meningitis complicating mumps, choriolymphocytic meningitis, pneumonia and infections polyneuritis. Is it true that all your patients with infectious polyneuritis recovered? Some of our patients have not. During poliomyelitis epidemics is there an increase in other virus infections?

DR. E. A. MORGAN, Toronto: Is lack of pain in the muscles invariable? I have at the present time a patient with a very typical condition who suffered acutely with muscular pain for two months. The pain was increased by passive movements. It was not merely hyperesthesia of the skin.

DR. F. W. JEFFREY, Ottawa: Does an increase in the cerebrospinal fluid cell count exclude the diagnosis of infectious polyneuritis? I had an infant 17 months of age with a condition diagnosed as infectious polyneuritis, with typical symptoms and showing some bulbar involvement and a cell count of 30 to 40, which disappeared in one week. The infant made an uneventful recovery in four months.

DR. C. E. SNELLING, Toronto: Is complete rest in bed essential in the treatment of these patients? How long should they be kept quiet, or is this necessary or advisable?

DR. H. B. CUSHING, Montreal: The good recovery that I described refers to recovery from the paralysis. If the patients suffer from widespread paralysis including some of the cranial nerves, they are likely to die from pneumonia and other complications. The early mortality in this disease is recognized. A definite percentage of the patients die. Even when there is widespread paralysis, there may be complete recovery if the patient survives the first few days. I do not know whether there is an increase in other virus infections during a poliomyelitis epidemic. Pain in the muscles may occur in this disease. One sees definite sensory disturbances in the skin in polyneuritis; these do not occur in poliomyelitis. I do not know whether an increase in spinal fluid cell counts may occur. After the acute painful stage has passed, complete rest is not essential. In fact, voluntary movements should be encouraged, as they help to maintain the nutrition of the muscles.

A Case of Extensive Root Resorption in Permanent Dentition. DR. E. A. MORGAN, Toronto.

A case of extensive root resorption of the permanent teeth is presented. The probable cause is orthodontic treatment, but the possibility of other etiologic factors is discussed. The incidence of this condition is presented, and a warning is issued that pediatricians should exercise some supervision over such treatment if they are alive to their responsibilities to their patients.

DISCUSSION

DR. A. P. HART, Toronto: For a number of years I have thought that the application of orthodontic appliances (bands) is dangerous, especially when they are used on permanent teeth. A tremendous amount of decay seems to be caused by bands when they are left on for years. It would seem advisable to put the bands on the first teeth and to correct the abnormality as much as possible before the second teeth appear. Great pressure had apparently been put on the bicuspids and incisors in this case, as they showed more change than the other teeth.

DR. ALTON GOLDBLOOM, Montreal: Orthodontists seem to be divided into two groups: (1) those who carry on the orthodontic treatment as early as possible on the first dentition, in order to develop the growth of the mandible, and (2) those who believe that the treatment should be delayed as long as possible and that the appliances should be left on for as short a time as possible. These orthodontists never straighten the primary teeth. These dentists start treatment when the patient is between 11 and 12 years old and finish it by the time he is

13 or so. They believe that when the appliances are put on early root resorption results. When they are applied late and for a short time, less resorption occurs. Had Dr. Morgan heard of this contrary view?

DR. E. A. MORGAN, Toronto: As far as Dr. Hart's question is concerned, this child had bands on both upper and lower teeth, and the pressure on the front teeth was pretty severe, but the molars are much less likely to show resorption than the incisors or bicuspids. In this case, part of the trouble was due to an over bite and part to an open bite. An open bite is not supposed to cause resorption, although it can cause infection about the teeth. The common cause of resorption is pressure. In regard to Dr. Goldbloom's remarks, the general opinion of the orthodontists, if one may judge from the recent literature, seems to be that the earlier orthodontic measures are instituted the less resorption will occur.

Health Insurance and the Pediatrician. DR. G. P. HAMBLIN, Toronto (by invitation) (paper read by Dr. E. Harkins).

Health insurance is a coming necessary step in social progress in Canada. Pediatricians, in leading the medical profession in preventive medicine, have in many respects already begun "health insurance." It is essential that they have an important voice in the designing of this new scheme. Research, in which department pediatricians have been foremost, is apt to be forgotten in such a sweeping change in medical practice, and it is important that they use every influence to maintain its role.

The medical profession has always been unselfish in promoting the welfare of the public. In asking the profession to increase its service at probably a reduced income, it is imperative to think also of "collective security" for physicians. The medical profession is one of the most insecure groups from the point of view of health, old age and dependent security. It behooves pediatricians to think and act collectively, not only for an increased status of national health but for a greater measure of social security for the profession and for the individual members.

Second Session

Saturday Afternoon

Use of Evaporated Half-Skimmed Milk in Infant Feeding. DR. C. E. SNELLING, Toronto.

One of the companies making evaporated milk has made available for the commercial market an evaporated partially skimmed milk, which when diluted with an equal amount of water makes a 2 per cent fat content milk.

Babies were fed on this in two nurseries for newborn infants, and comparison was made with feedings of equal caloric content of regular evaporated milk.

The results with the partially skimmed milk show that it is better tolerated and that the babies make a better weight gain on it.

DISCUSSION

DR. T. G. H. DRAKE, Toronto: This new evaporated partially skimmed milk is handled by the grocers and is not higher priced than the usual evaporated milk.

DR. ALTON GOLDBLOOM, Montreal: I do not prescribe such dilute mixtures as Dr. Snelling does during the newborn period. I put the babies on either 12 ounces (360 cc.) of whole milk, 8 ounces (240 cc.) of water and 1 ounce (30 Gm.) of sugar or 6 ounces (180 cc.) of evaporated milk, 14 ounces (420 cc.) of water and 1 ounce (30 Gm.) of sugar. The same formula can be used throughout the newborn period. I do not believe it is necessary to start with 1 ounce of milk and work up gradually. Partially skimmed evaporated milk is a boon in many ways in infant feeding. Levine and Gordon, working under the auspices of the National Institute of Health, and Emmett Holt Jr. have shown that for pre-

mature infants it is necessary to reduce the fat both in human milk and in other milks and to add ascorbic acid, as this substance assists the body to digest completely certain of the essential amino acids. Since the work of Levine and Gordon and Holt, I have been sufficiently impressed by their results and my own to use the partially skimmed evaporated milk and ascorbic acid for premature infants from the first day.

Dr. E. B. Harkins, Toronto: According to the experience in one nursery for newborn infants in Toronto, full strength evaporated milk feedings in the strength advocated by Dr. Goldbloom give rise to some digestive disturbances. The feedings were therefore changed to 2 per cent skim milk mixtures, which improved the situation considerably. This new product is of value because it combines the advantages of a low fat feeding with those of evaporated milk. I hope the results will be better than those obtained with full strength evaporated milk or 2 per cent milk. I do not use as low dilutions as Dr. Snelling does in the early newborn period. I did run into trouble frequently when I used a mixture of 6 ounces (180 cc.) of evaporated milk, 15 ounces (450 cc.) of water and 1 ounce (30 Gm.) of sugar.

Dr. S. J. Usher, Montreal: Not infrequently one sees a baby that is doing nicely and gaining steadily, but the mother complains that the baby always regurgitates the last mouthful of its feeding and always smells sour.

Dr. C. E. Snelling, Toronto: With these newborn infants, if the feeding is too strong a break in tolerance may occur in a day or two, as indicated by diarrhea. The feedings during the newborn period which were outlined are much like the routine feedings used in the Toronto General Hospital and the Toronto Western Hospital. In the first few days of life, fluids are of more importance than calories, and it is safer to increase the calories slowly. In regard to the regurgitation described by Dr. Usher, if one reduces the fat in the feeding one eliminates a great deal of regurgitation in certain babies.

Dr. R. R. Struthers, Montreal: Years ago, skimmed milk was advocated as the best feeding for newborn infants. If too strong a mixture of evaporated milk is used in the newborn period, regurgitation, diarrhea and scalded buttocks are apt to occur. My experience agrees with Dr. Snelling's, that it is better to use skimmed milk rather than dilutions of evaporated milk in the newborn period. In Montreal this new type of evaporated milk is sold by the druggists.

Dr. C. E. Snelling, Toronto: The grocers certainly handle it in Toronto, and one could no doubt, if one requested it, have them sell it in Montreal also.

Extragenital Primary Syphilis Treated by Massive Doses of Mapharsen.

Dr. Alton Goldbloom and Dr. Paul Hardy (by invitation), Montreal.

Treatment of acquired extragenital syphilis with massive doses of mapharsen for five days was used for the first time at the Montreal Children's Hospital for 2 children, a boy and a girl, aged 2 and 3 years respectively. The boy, aged 2 years, received 300 mg. of mapharsen by the intravenous drip method, and the girl, aged 3 years, received 400 mg. of mapharsen over a similar period. The lesion healed promptly, and the Wassermann titer fell from positive 1 in 256 to positive 1 in 12 within a month. The patients are still under observation. The first patient, who received the smaller dose, had a local recurrence, which was subsequently treated by the older methods. The second patient has remained symptom free. Vomiting and a moderate febrile reaction were the only untoward symptoms.

DISCUSSION

Dr. E. A. Morgan, Toronto: The child with acquired syphilis responds as well to antisyphilitic treatment as the adult if it is started early in the disease. However, I should like to warn against the dangers of massive dose treatment of congenital syphilis. There is quite a different situation in a 2 month old child

with congenital syphilis than in a person who has recently acquired syphilis. In congenital syphilis there is a generalized infection, as can be easily seen by examining the viscera post mortem. Intravenous arsenic is therefore dangerous. A 2 month old infant stands small doses of arsenic once a week poorly. No doubt many syphilitic children have died as the result of intravenous administration of arsenic compounds, even in small doses. One cannot use massive dose treatment in early congenital syphilis. In the late stages of congenital syphilis, no results follow massive treatment. The course of the Wassermann reaction in Dr. Goldbloom's second case is suggestive of the following type of case. Not infrequently pediatricians see children who come at the age of 5 or 6 years with a 3-2-1 Wassermann reaction. The reaction becomes 4-4-4 after a few treatments and persists at that level for two or three years. This is similar to the well known provocative test in cases in which the reaction is negative. I have encountered only 5 cases of acquired syphilis in children in the last twenty-five years. Two of the children had lesions on the lip, 1 on the scalp and 2 on the genital organs. Acquired syphilis is certainly not commonly seen in children. The next patient that I see will be given massive dose treatment. The five day massive dose treatment with mapharsen seems to be falling into disrepute to some extent, because relapses are commoner after it than after the usual arsphenamine or neoarsphenamine series. Such a relapse occurred in Dr. Goldbloom's first case.

DR. R. R. STRUTHERS, Montreal: Some time ago I treated a 4 Kg. 1 month old baby suffering from congenital syphilis with mapharsen by the massive dose method. On the first day the infant received 5 mg. per kilogram; on the second day, 10 mg. per kilogram, and on each of the next three days, 15 mg. per kilogram. The clinical results were good, and there were apparently no untoward effects. From Dr. Morgan's description, I am afraid that its organs may have been injured, though time alone will tell that.

A Comparative Study of S. M. A., Evaporated Milk and Breast Milk Feedings. DR. K. L. MCALPINE and DR. GEORGE SUMNER (by invitation), London, Ontario.

This investigation was conducted to study and compare a series of infants in the first year of life fed breast milk, evaporated milk and S. M. A., and especially to determine the protein sufficiency of S. M. A. Sixty-eight babies were followed, of whom 52 were available for final analysis. The weight curve for the group fed S. M. A. was slightly lower than that for the group fed evaporated milk. However, infants given S. M. A. showed a greater gain while solely on milk feedings, prior to the introduction of solid food. Hemoglobin determinations revealed each group to be free of nutritional anemia. The fortification of S. M. A. by added iron was without demonstrable effect on hemoglobin synthesis. The evaluation of tissue turgor of the group fed S. M. A. compared favorably with that of the infants fed at the breast and on evaporated milk. No unusual difficulties were encountered concerning food tolerance of either group, nor was there any significant difference regarding infections of the respiratory tract. Roentgenologic studies demonstrated that S. M. A. and irradiated evaporated milk contained sufficient vitamin D to protect against rickets in the average full term infant. From clinical evaluation, S. M. A. was considered to contain adequate protein. Evaporated milk and S. M. A. were regarded as satisfactory foods for the majority of infants.

DISCUSSION

DR. H. S. LITTLE, London: I examined a fair number of the babies who were being fed S. M. A., and they certainly were splendid specimens. They had good tissue turgor and no signs of anemia. It appears that S. M. A. has a definite place in infant feeding during the first two or three months, but after that other foods are equally well tolerated. Quite a number of physicians in the London

district are using S. M. A. Several cases of scurvy have appeared among the babies fed this preparation. This is due to no fault of the producers, as they specifically state that the product contains no vitamin C and that this vitamin must be administered as well. The fact that they point out its similarity to breast milk, however, might lead to a false feeling of security as far as vitamin C is concerned.

DR. T. G. H. DRAKE, Toronto: I should like to inquire regarding the relative cost of S. M. A. and other common foods.

DR. A. P. HART, Toronto: I was struck by the difference in the iron content of the feedings. I think it is a good idea to give iron. I sometimes think the giving of iron in infant feeding is frequently neglected.

DR. S. J. USHER, Montreal: I was interested to note that the added iron in the S. M. A. was of no additional advantage as far as a further increase in production of hemoglobin was concerned. In a study of 400 infants in an orphanage, it was found that those 4 to 5 months of age had a hemoglobin level of 60 to 70 per cent and that those 1 year of age had a level of 60 per cent. These infants had frequent infections and were not comparable to those of Dr. McAlpine's series, but even when large doses of iron or iron and copper together were given, the hemoglobin level rarely rose above 80 per cent in infants who were from 4 to 12 months old.

DR. E. CHANT ROBERTSON, Toronto: I noticed that the average weight of the babies fed S. M. A. was 7½ pounds (3,402 Gm.), whereas the average weight of those given evaporated milk was 9 pounds (4,082 Gm.). Would not the smaller babies tend to grow more rapidly? It appears doubtful, therefore, that the more rapid growth of the babies fed S. M. A. during the first few months was of significance.

DR. C. E. SNELLING, Toronto: In regard to low protein feedings in premature infants, when premature infants were fed pooled breast milk alone they did very well at first and gained weight exceptionally rapidly. However, they were prone to have serious diarrhea when on this feeding, and many of them died subsequently. In my experience, similar results were obtained with S. M. A. Premature infants under my care are now given a feeding made of 2 parts of boiled breast milk and 1 part of protein milk. This feeding is lower in calories and leads to slower weight gains, but the mortality rate is not nearly as high as when breast milk alone is used. The boiling and handling of the breast milk reduces its protein content, most of which is lactalbumin. The poorer results with breast milk only may be due to this reduction in its proteins. The addition of protein milk to the breast milk compensates for this deficiency. I wonder if the low percentage of protein in S. M. A. was what caused it to be found unsatisfactory as a feeding for premature infants. Better results were obtained with S. M. A. protein milk.

DR. K. L. MCALPINE, London, Ontario: After 2 or 3 months of age, there was little difference in the weight gains of the babies fed S. M. A., evaporated milk and breast milk. Furthermore, it was impossible to determine differences in tissue turgor between these groups at any time during the course of the experiment. In regard to the relative cost of the different feedings, S. M. A. is more expensive than evaporated milk, but if the baby is being fed a formula containing dextrimaltose and also some source of vitamin D, the expense is about the same as for S. M. A. In regard to hemoglobin formation, one would expect the hemoglobin levels to be higher in the babies fed S. M. A., because a certain amount of iron and ammonium citrates has been added to it. However, this was not the case. Apparently all the babies already had optimum hemoglobin levels. It is true that lighter infants tend to gain in weight more rapidly than heavier ones. The more rapid early gains of the babies fed S. M. A. may have been due to their lighter average weights.

A Syndrome of Cutaneous Fragility and Hyperlaxity and Articular Hyperlaxity. Dr. Benjamin Benjamin (by invitation) and Dr. R. R. Struthers, Montreal.

Instances of a syndrome characterized by cutaneous fragility, hyperelasticity and hyperlaxity and articular hyperlaxity have been reported by a number of authors. It is apparently uncommon. There is usually a tendency to easy bruising associated with it, and the production of hematomas and raisin-like elevations of the skin may take place. Thin papyraceous scars frequently develop at the sites of cutaneous lacerations, especially over bony prominences. Nothing is known regarding the cause of the condition. That it might result from a congenital anomaly of mesenchyme seems likely. The only consistent histopathologic state noted in biopsy specimens of skin is an increased and abnormal distribution of elastic tissue. Prevention of injury is all that can be advised in the way of treatment. A case of the typical complete syndrome in a 7 year old girl has been described. A second case, which, though the syndrome was incomplete, probably belongs in the same category, was observed. The patient was a 9 year old girl in whom there was pronounced cutaneous fragility with multiple tissue paper–like scars, but no clinical evidence of extreme elasticity of the skin or hyperlaxity of joints.

Ascorbic Acid Content of Fruits and Vegetables. Miss W. M. Johnstone, Toronto; Dr. J. H. L. Truscott (by invitation), London, Ontario, and Dr. T. G. H. Drake, Toronto.

To supply the daily allowance of ascorbic acid recommended by the Committee on Food and Nutrition of the National Research Council, Washington, D. C., the intake of food containing this vitamin cannot be left to chance. Vegetables bought retail on the same day in different stores showed wide variations in ascorbic acid content. Shading during growth decreases the vitamin C content of tomatoes and of head lettuce. During storage, even at 32 F., the loss of vitamin C is rapid in spinach, green beans, head lettuce, asparagus and other vegetables. Asparagus stored at room temperature for four days lost 80 per cent of its ascorbic acid content. Asparagus purchased at the farmers' market, Toronto, contained nearly twice as much vitamin C as did asparagus purchased in retail stores. Over the year, fresh orange juice averaged 51 mg. and fresh grapefruit juice 43 mg. of ascorbic acid per hundred grams. Of the canned fruit and vegetable juices, grapefruit juice is the cheapest source of vitamin C. Canned tomatoes and tomato juices processed at Vineland Experimental Station, Ontario, contained 58 per cent more ascorbic acid than the average of commercially canned specimens. The ascorbic acid of potatoes, apples and many other fruits and vegetables is practically all destroyed in one or two minutes after the raw material is finely divided by fine grating, grinding or juicing. This rapid oxidase reaction does not occur in the case of citrous fruits or raw tomatoes.

DISCUSSION

Dr. A. P. Hart, Toronto: I was particularly interested in the amount of vitamin C in potatoes. I remember that Dr. Still thirty years ago treated all his patients with scurvy with baked potato. It sometimes seemed about as effective as orange juice. I often wondered how it cured them, because vitamin C was believed to be destroyed by heat; but it is now known that potatoes contain good amounts of vitamin C and that baking is the best way to cook them to preserve this vitamin.

Dr. E. A. Morgan, Toronto: If orange juice is squeezed the night before and left in the refrigerator, will it have lost much ascorbic acid by the next day?

Dr. T. G. H. Drake, Toronto: Orange juice prepared from fresh oranges or tomato juice prepared from canned tomatoes loses practically no vitamin C on

standing twenty-four hours in the refrigerator. This is due to the fact that these foods do not contain the vitamin C–destroying oxidases.

Allergic Asthma: Mixed Inhalant Therapy. Dr. H. E. Edwards (by invitation), Toronto.

A series of 24 patients with allergic asthma were treated with a mixture of equal parts of duck feathers, house dust, sheep wool and cattle hair. These were among the most frequently offending allergens found in 122 asthmatic patients giving positive reactions to cutaneous tests. All 24 patients were sensitive to one or more allergens of the mixture, 83 per cent being sensitive to two or more. Eighty-three per cent of the patients were benefited definitely, and in 62.5 per cent the results were good or excellent. It is submitted that mixed inhalant therapy for allergic asthma is a useful procedure for clinics where large numbers of patients are seen.

DISCUSSION

Dr. G. A. Campbell, Ottawa: Theophylline with ethylenediamine is by long odds the best drug available for the relief of asthma.

Dr. E. B. Harkins, Toronto: The tablets used in the Hospital for Sick Children are much better for administration to younger asthmatic patients than the capsules prepared commercially, which are usually hard to administer. It would be a great advantage if a similar tablet were on the market.

Dr. T. G. H. Drake, Toronto: What is the composition of the tablet that you used?

Dr. H. E. Edwards, Toronto: The tablets we used contained 2½ grains (0.16 Gm.) of theophylline with ethylenediamine, 0.375 grain (0.025 Gm.) of ephedrine hydrochloride and 0.25 grain (0.016 Gm.) of phenobarbital.

Recurrent Toxic Goiter with Chorea. Dr. S. J. Usher, Montreal.

A case of persistent thyrotoxicosis in a 15 year old girl is reported. This has been present for about three years, despite two operations on the thyroid. The increased basal metabolic rate has been controlled to a great extent by the use of compound solution of iodine (Lugol's solution), which, however, has had no effect on curing the underlying condition. During the period of observation there have been two intercurrent attacks of chorea. The first of these was severe and was followed within a week by an attack of paratyphoid fever lasting two weeks. The fever had a beneficial effect on the choreiform movements. The second attack of chorea, which was less severe, was rapidly alleviated when the increased metabolic rate was lowered by the use of the iodine solution. Electroencephalograms have shown generalized cerebral dysrhythmia of a mixed type, exhibiting the changes present in both chorea and thyrotoxicosis. The heart has remained comparatively uninvolved, there being only slight cardiac enlargement and no murmurs.

Value of Ultraviolet Rays in Reducing Cross Infections of the Respiratory Tract in Hospital Wards. Dr. Elizabeth Chant Robertson, Toronto, and Miss M. E. Doyle (by invitation), Toronto.

In infants under 6 months of age treated in a room divided into six cubicles by complete partitions at the sides, but open at the front, nearly as many cross infections of the respiratory tract developed as in similar infants in an open six bed room, or in a room with partitions extending from the floor to two feet below the ceiling. Nine changes per hour of fresh air were introduced into the first room; in the other rooms the ventilation was by windows and a transom above the door. When ultraviolet ray lamps were mounted around the cubicle entrances in the completely partitioned, artificially ventilated room, the babies

acquired one third as many infections of the respiratory tract as those in the open room and one half as many infections as those in the partially partitioned room. The curtains of ultraviolet rays therefore seem to be the most important factor in preventing such infections.

In one of the rooms in which premature infants were treated, ultraviolet ray lamps were suspended from the ceiling and reflected upward, so that the upper air was irradiated. In this room, in which the doors and windows were always kept closed, infections were about half as numerous as in a similar unirradiated room for premature infants. Two other rooms used for older infants, in which there was similar irradiation but the doors and windows were often left open, had as high an incidence of infections as the control rooms.

Material from the throat and nose was frequently taken for culture. Sixty-seven strains of group A hemolytic streptococci (all but 7 typable) and 104 strains of pneumococci were isolated from 674 babies. Seventy-five strains of group A hemolytic streptococci (all but 7 typable) and 30 strains of pneumococci were isolated from the personnel (291 in number) treating these infants. In only 18 instances were these organisms shown to be transferred from patient to patient or from patient to attendant or vice versa.

Book Reviews

Pediatric Gynecology. By Dr. Goodrich C. Schauffler. Price, $5.00. Pp. 384, with 66 illustrations. Chicago: The Year Book Publishers, Inc., 1942.

The author's particular interest in the field of pediatric gynecology dates back to 1925, when, confronted with a gynecologic problem in a girl of 3 years, he discovered how poorly this field was covered in the medical literature. He is now assistant clinical professor of obstetrics and gynecology at the University of Oregon Medical School and brings a wealth of clinical experience to his presentation of the subject. He keeps in mind throughout the pediatric, psychiatric, gynecologic and surgical approaches to the various problems, so that his contribution is of great value to all four branches of medicine. The book is well written and excellently illustrated.

The scope of the book is broader than might be expected from the title. Considerable attention is given to psychologic factors in management, and there is a chapter on the social service aspects, written in collaboration with Mary L. Eggleston, and one on the medicolegal aspects, written in collaboration with Dan H. Northrup and Stuart R. Stimmel. Before the author discusses any of the pathologic conditions affecting the female genital organs, he gives a thorough presentation of the normal anatomy and physiology. There are chapters on the pelvic viscera and general surgical consideration, written in collaboration with C. W. Brunkow, a chapter on urologic aspects, with Elmer Belt as collaborator, and a chapter on proctologic considerations, with Donald R. Laird as collaborator. The appendix includes basic standards of hormone units, a list of commercial endocrine preparations and a list of state agencies administering services under title V, parts 1, 2 and 3 of the Social Security Act. The index is well prepared.

Family Nutrition. By Rachel M. Winlock, M.D.; Emerson R. Sausser, D.D.S.; Joseph Stokes, Jr., M.D.; James J. Waygood, M.D.; Anna de Planter Bowes, M.A., and Pauline Beery Mack, Ph.D. Price, free. Pp. 112, with 27 illustrations. Philadelphia: The Philadelphia Child Health Society, 1942.

The committee which prepared this monograph on family nutrition for the Philadelphia Child Health Society consisted of four physicians, one dentist and two nutritionists. A grant from the Beneficial Industrial Loan Corporation has made possible its free distribution on request.

The incorporated reports of studies on nutritional fitness show the need for just the kind of information the remainder of the monograph provides. There is an excellent discussion of the dietary values of common foods and of the nutritional needs of adults and children. The larger portion of the book is given over to showing how these needs may be met in families of different income levels. There is no index, but the material is so arranged in tables and under large type headings that one can find easily the desired information.

Etiopatogenia de la enfermedad celiaca: Monograph No. 7. Facultad de Medicina de Montevideo. By A. Munilla. Price, not given. Pp. 32, with 7 figures. Montevideo: A. Monteverde & Cia, 1942.

A concise résumé of the etiology of celiac disease is given and is followed by reports of the author's own experiments, in which he was able to induce abdominal distention, steatorrhea and osteoporosis in white rats by the injection of iodoacetate subcutaneously. Histologic sections are reproduced in which it is shown that these conditions are due to changes in the intestinal mucosa and an inability to absorb fats. He was also able to obtain similar results with adrenalectomized rats. This is an excellent piece of work and is well written.

Directory of Pediatric Societies*

INTERNATIONAL

International Association of Preventive Pediatrics

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
General Secretary: Dr. Kenneth D. Blackfan, 300 Longwood Ave., Boston.
Assistant Secretary-Treasurer: Dr. Charles F. McKhann, University of Michigan, Ann Arbor, Mich.

Canadian Committee:

Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St. W., Montreal.
Place: Boston. Time: Postponed indefinitely.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

FOREIGN

Argentine Pediatric Society of Buenos Aires

President: Dr. Martin Ramón Arana, 1809 Rodriguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Larguia, Cerrito 1179, Buenos Aires.

British Pediatric Association

President: Prof. Charles McNeil, 44 Heriot Row, Edinburgh, Scotland.
Secretary: Dr. Arthur G. Maitland Jones, 31A Weymouth St., London, W. 1.

Danish Pediatric Society

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. E. Gjørup, Dronning Louises Børnehospital, Copenhagen.

Nederlandische Vereeniging voor Kindergeneeskunde

President: Dr. J. H. G. Carstens, Servaasbolwerk 14ª, Utrecht.
Secretary: Dr. R. P. van de Kasteele, Laan van Poot 340, 's Gravenhage.
Place: Different places. Time: Three times a year.

Paediatrický Spolok na Slovensku

President: Dr. A. J. C. Chura, Lazaretská 11, Bratislava.
Secretary: Dr. P. Rados, Lazaretská 6, Bratislava.
Place: Pediatric Clinic, University Bratislava. Time: Six times a year.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. E. A. Cockayne, 98 Harley St., London, W. 1, England.
Secretary: Dr. R. Lightwood, 86 Brook St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p.m.

*Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

PALESTINE JEWISH MEDICAL ASSOCIATION, SECTION OF PHYSICIANS OF CHILDREN'S DISEASES

President: Prof. S. Rosenbaum, 26 Bialkstr., Tel Aviv.
Secretar: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

SOCIEDAD CUBANA DE PEDIATRÍA

President: Dr. Clemente Inclan Costa, Marique 48, Habana.
Secretary: Dr. Serafin Falcon Lopez, Calle B No. 356, Velado, Habana.
Place: Cátedra de Clinica Infantil, Hospital Mercedes, Habana. Time: Last Wednesday of every month.

SOCIEDAD MEXICANA DE PEDIATRIA

President: Dr. Fernando López Clares, 12/a. Medellín 191, Mexico City.
Secretary: Dr. Jesus Gómez Pagola, Versalles 64, Mexico City.

SOCIEDAD VENEZOLANA DE PUERICULTURA Y PEDIATRIA

President: Dr. Ernesto Vizcarrondo, Venezuela.
Secretary: Dr E. Santos Mendoza, Venezuela.

SOCIÉTÉ DE PÉDIATRIE DE PARIS

President: Dr. B. Weill-Hallé, 49 Avenue Raymond Poincare, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Malades, 49 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

URUGUAYAN SOCIETY OF PEDIATRICS

President: Dr. Conrado Pelfort, Ave 18 de Julio 1246, Montevideo.
Secretary: Dr. Héctor Mourigan, Ave 18 de Julio 2175, Montevideo.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON PEDIATRICS

Chairman: Dr. Hugh L. Dwyer, 315 Alameda Rd., Kansas City, Mo.
Secretary: Dr. Gilbert J. Levy, 188 S. Bellevue Blvd., Memphis, Tenn.
Place: San Francisco.

AMERICAN ACADEMY OF PEDIATRICS

President: Dr. Edward C. Mitchell, 1073 Madison Ave., Memphis, Tenn.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Place: Palmer House, Chicago. Time: Nov. 4-7, 1942.
Region IV. Meeting cancelled.

AMERICAN HOSPITAL ASSOCIATION, CHILDREN'S HOSPITAL SECTION

Chairman: Dr. D. L. Richardson, 593 Eddy St., Providence, R. I.
Secretary: Dr. Joelle C. Hiebert, 299 Main St., Lewiston, Maine.

AMERICAN PEDIATRIC SOCIETY

President: Dr. Edwards A. Park, Johns Hopkins Hospital, Baltimore, Md.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. L. M. Lindsay, 815 Medical Arts Bldg., Montreal.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, Hospital for Sick Children, Toronto.

SOCIETY FOR PEDIATRIC RESEARCH

President: Dr. George M. Guest, Children's Hospital, Cincinnati.
Secretary: Dr. Mitchell I. Rubin, 1740 Bainbridge St., Philadelphia.

SECTIONAL

INTERMOUNTAIN PEDIATRIC SOCIETY

President: Dr. Eugene Smith, 385–24th St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. R. Cannon Eley, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. James Marvin Baty, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. M. L. Bridgeman, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. C. G. Ashley, 833 S. W. 11th Ave., Portland, Ore.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. G. R. Fisher, 23 E. Pikes Peak Ave., Colorado Springs, Colo.
Secretary: Dr. Joseph H. Lyday, 1850 Gilpin St., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 2:30 p. m.

SOUTHERN MEDICAL ASSOCIATION, SECTION OF PEDIATRICS

Chairman: Dr. George M. Lyon, 955–4th Ave., Huntington, W. Va.
Secretary: Dr. William Weston Jr., 1428 Lady St., Columbia, S. C.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. M. V. Adams, 803 Government St., Mobile.
Secretary-Treasurer: Dr. William R. Britton, 4 Catoma St., Montgomery.

ARIZONA PEDIATRIC SOCIETY

President: Dr. Vivian Tappan, San Clemente, Tucson.
Secretary: Dr. Hilda Kroeger, Arizona State Health Dept. (Maternal and Child Welfare Division), Phoenix.

ARKANSAS STATE PEDIATRIC ASSOCIATION

Chairman: Dr. C. B. Billingsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

CALIFORNIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. William Belford, 233 A St., San Diego.
Secretary: Dr. John J. Miller Jr., 2398 Sacramento St., San Francisco.

FLORIDA STATE PEDIATRIC SOCIETY

President: Dr. Ludo Von Meysenbug, Box 3356, Daytona Beach.
Secretary: Dr. Robert Blessing, 409 Blount Bldg., Ft. Lauderdale.
Place: Concurrent with state association meeting at time of convention.

Georgia Pediatric Society

President: Dr. Frank Schley, 1301 Broadway, Columbus.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. Ernest Caulfield, 683 Asylum Ave., Hartford.
Secretary: Dr. Edward T. Wakeman, 129 Whitney Ave., New Haven.
Time: Three meetings a year.

Illinois State Medical Society, Section on Pediatrics

Chairman: Dr. Craig D. Butler, 715 Lake St., Oak Park.
Secretary: Dr. A. J. Fletcher, 139 N. Vermilion, Danville.

Indiana State Pediatric Society

President: Dr. K. T. Knode, 1105 E. Jefferson Blvd., South Bend.
Secretary-Treasurer: Dr. Mathew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

Iowa Pediatric Society

President: Dr. Mark L. Floyd, Children's Hospital, Iowa City.
Secretary-Treasurer: Dr. James Dunn, Davenport Bank Bldg., Davenport.

Louisiana State Pediatric Society

President: Dr. S. G. Wolfe, 1560 Line Ave., Shreveport.
Secretary-Treasurer: Dr. W. C. Rivenbark, 1448 Louisiana Ave., New Oleans.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Norman L. Hawkins, 11 Public Sq., Watertown, N. Y.
Secretary: Dr. William J Orr, 135 Linwood Ave., Buffalo.

Medical Society of the State of Pennsylvania, Pediatric Section

Chairman: Dr. John D. Sturgeon Jr., 22 N. Gallatin Ave., Uniontown.
Secretary: Dr. Elwood W. Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Place: Pittsburgh. Time: Sept. 29-Oct. 2, 1942.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. Harry Towsley, University of Michigan Hospital, Ann Arbor.
Secretary: Dr. Leon DeVel, 110 E. Fulton, Grand Rapids.

Mississippi State Pediatric Society

President: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Secretary: Dr. Guy Verner, 126 N. Congress St., Jackson.

Nebraska Pediatric Society

President: Dr. Andrew G. Dow, 314 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John M. Thomas, 301 N. 49th St., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

New Hampshire Pediatric Society

President: Dr. MacLean J. Gill, 14 N. State St., Concord.
Secretary-Treasurer: Dr. Ursula G. Sanders, 46 Pleasant St., Concord.
Time: Twice yearly.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Thomas M. Watson, Greenville.
Secretary: Dr. Frederick B. Haar, Greenville.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. Ben H. Nicholson, 301 N. W. 12th St., Oklahoma City.
Secretary: Dr. Luvern Hays, 108 W. 6th St., Tulsa.
Place: Oklahoma Club. Time: 6:30 p. m., fourth Friday of each alternate month from September to May, inclusive.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. R. B. Josey, 1517 Hampton Ave., Columbia.
Secretary-Treasurer: Dr. Wilson Ball, South Carolina State Health Dept., Columbia.

TENNESSEE STATE PEDIATRIC SOCIETY

President: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.
Secretary: Dr. Gilbert Eblen, 611 W. Main Ave., Knoxville.

TEXAS PEDIATRIC SOCIETY

President: Dr. P. E. Luecke, 4105 Live Oak St., Dallas.
Secretary-Treasurer: Dr. John Ashby, 3610 Fairmount Ave., Dallas.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. John M. Bishop, 511 Medical Arts Bldg., Roanoke.
Secretary: Dr. Edwin A. Harper, 301 Rivermont Ave., Lynchburg.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. Theresa O. Snaith, 450 Center Ave., Weston.
Secretary: Dr. Henrietta L. Marquis, 211 Bair Bldg., Beckley.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. J. D. Nourse, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. I. B. Silber, 10465 Carnegie Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time October, December, February and April.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. I. Nelles Silverthorne, 170 St. George St., Toronto, Canada.
Secretary: Dr. G. P. Hamblin, 2333 Bloor St. W., Toronto, Canada.

BRONX PEDIATRIC SOCIETY

President: Dr. David Zahn, 2474 Valentine Ave., New York.
Secretary: Dr. Harry J. Cohen, 975 Walton Ave., New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

BROOKLYN ACADEMY OF PEDIATRICS

President: Dr. Paul L. Parrish, 52 S. Oxford St., Brooklyn.
Secretary: Dr. Lewis A. Koch, 62 Pierrepont St., Brooklyn.
Place: Granada Hotel. Time: Fourth Wednesday of each month, except May, June, July, August and September.

Buffalo Pediatric Society

President: Dr. A. Wilmot Jacobsen, 187 Bryant St., Buffalo, N. Y.
Secretary: Dr. Richard A. Downey, 786 Forest Ave., Buffalo, N. Y.
Place: Children's Hospital, 219 Bryant St. Time: 8:30 p. m., first Monday of each month from September to June.

Central New York Pediatric Club

President: Dr. Frank van der Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Places: Various cities in New York. Time: Third Tuesday of April and September.

Chicago Pediatric Society

President: Dr. James H. Wallace, 715 Lake St., Oak Park, Ill.
Secretary: Dr. Henry G. Poncher, 1819 W. Polk St., Chicago.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

Cincinnati Pediatric Society

President: Dr. Lloyd K. Felter, 3144 Jefferson Ave., Cincinnati.
Secretary: Dr. Leo S. Friedman, 3586 Reading Rd., Cincinnati.
Place: Children's Hospital, Elland Ave., Cincinnati. Time: On call.

Dallas Pediatric Society

President: Dr. Bruce A. Knickerbocker, 3403 Hall St., Dallas, Texas.
Secretary-Treasurer: Dr. Floyd A. Norman, 4325 Cole Ave., Dallas, Texas.
Place: Bradford Baby Hospital. Time 1 p. m., second and fourth Saturdays of each month.

Detroit Pediatric Society

President: Dr. Hugh Lewis, Detroit, Mich.
Secretary: Dr. John J. Pollack, 622-26 Maccabees Bldg., Detroit, Mich.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

Fulton County Medical Society, Pediatrics Section (Atlanta, Ga.)

Chairman: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.
Secretary: Dr. Harry Lange, 478 Peachtree St. N. E., Atlanta.
Place: Academy of Medicine, 38 Prescott St. N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Houston Pediatric Society

President: Dr. Raymond Cohen, 2300 Caroline St., Houston, Texas.
Secretary: Dr. Betty Moody, 526 Richmond Rd., Houston, Texas.
Place: College Inn. Houston. Time: Fourth Monday of each month.

Kansas City (Missouri) Pediatric Society

President: Dr. Edwin H. Schorer, 1103 Grand Ave., Kansas City.
Secretary: Dr. H. E. Petersen, Physicians and Surgeon's Bldg., St. Joseph, Mo.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. Alonzo Cass, 1908 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Gladys Patric Shahovitch, 3936 Roderick Rd., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd. Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Irwin Schiff, 658 Eastern Parkway, Brooklyn.
Secretary: Dr. Henry Rascoff, 895 Eastern Parkway, Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m., fourth Monday of each month, October to April, inclusive.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. Meyeron Coe, 217-02–91st Ave., Queens Village, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144–38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Medical Society of the District of Columbia, Section on Pediatrics

President: Dr. James M. Moser, 3751 Jenifer St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. William A, Howard, 2222 Que St. N. W., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time: 8 p. m., fourth Thursday of every month.

Memphis Pediatric Society

President: Dr. E. C. Mitchell, 1073 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: John Gaston Hospital. Time: Quarterly.

Milwaukee Pediatric Society

President: Dr. John H. Reynolds, 1628 W. Wisconsin Ave., Milwaukee.
Secretary-Treasurer: Dr. F. J. Mellencamp, 324 E. Wisconsin Ave., Milwaukee.
Place: Milwaukee Athletic Club. Time: Second Wednesday of each alternate month, beginning with February.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Alfred Langmann, 108 E. 68th St., New York.
Secretary: Dr. Edith M. Lincoln, 600 Park Ave., New York.
Place: New York Academy of Medicine, 2 E, 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northern California Affiliates

President: Dr. Crawford Bost, 490 Post St., San Francisco.
Secretary: Dr. William A Reilly, 384 Post St., San Francisco.
Time: Second Thursday of September, November, January, March and May.

Northwestern Pediatric Society

President: Dr. John M. Adams, 1009 Nicollet Ave., Minneapolis.
Secretary-Treasurer: Dr. Albert V. Stoesser, 205 W. University Hospital, Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Oklahoma City Pediatric Society

President: Dr. J. Byron Snow, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 1200 N. Walker St., Oklahoma City.
Place: Oklahoma Club. Time: Fourth Friday of each alternate month.

Philadelphia Pediatric Society

President: Dr. Paul B. Cassidy, 2037 Pine St., Philadelphia.
Secretary: Dr. Aims C. McGuinness, Children's Hospital, 1740 Bainbridge St., Philadelphia.
Place: College of Physicians, 19 S. 22d. St. Time: Second Tuesday of each month from October to April, inclusive.

Pittsburgh Pediatric Society

President: Dr. Carl Ruder, 646 Washington Rd., Mount Lebanon, Pittsburgh.
Secretary-Treasurer: Dr. C. J. Stoecklein, 125 De Soto St., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate month from October to June, inclusive.

Richmond Pediatric Society

President: Dr. Stanley Meade, 913 Floyd Ave., Richmond, Va.
Secretary-Treasurer: Dr. Herman W. Farber, 501 E. Franklin St., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: 8 p. m., third Thursday of each month, except June, July and August.

Rochester Pediatric Society

President: Dr. Herbert Soule, 122 Rutgers St., Rochester, N. Y.
Secretary-Treasurer: Dr. Jerome Glaser, 300 S. Goodman St., Rochester, N. Y.
Place: Rochester Academy of Medicine or arrangement by program committee. Time: Third Friday of each month from October to May.

St. Louis Pediatric Society

President: Dr. Maurice J. Lonsway, 3720 Washington Blvd., St. Louis.
Secretary-Treasurer: Dr. Mary A. McLoon, 408 Humboldt Bldg., St. Louis.
Place: St. Louis Medical Society Bldg. Time: First Friday of each month from October to June.

Seattle Pediatric Society

President: Dr. Frederick B. Joy, Stimson Bldg., Seattle.
Secretary: Dr. Sherod M. Billington, Medical Dental Bldg., Seattle.
Place: College Club. Time: Third Friday of each month from September to June at 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Paul Hamilton, 1635 Chelsea Rd., San Marino, Calif.
Secretary: Dr. Helen Hopkins, 3875 Wilshire Blvd., Los Angeles.
Place: Jonathan Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Campbell Harvey, 35 W. Huron St., Pontiac, Mich.
Secretary: Dr. Harry A. Towsley, University of Michigan, Department of Pediatrics and Communicable Diseases, Ann Arbor, Mich.

Westchester County Medical Society, Pediatrics Section (New York)

President: Dr. John B. Ahouse, 27 Ludlow St., Yonkers, N. Y.
Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Rd., Rye.
Place: Grasslands Hospital, Valhalla, N. Y. Time: Third Thursday in October, December, February and April.